IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IMMUNEX CORPORATION; AMGEN MANUFACTURING, LIMITED; and HOFFMANN-LA ROCHE INC.;	)	Hon. Claire C. Cecchi
Plaintiffs, v.	)	Civil Action No.: 2:16-cv-01118-CCC-MF
SANDOZ INC.; SANDOZ INTERNATIONAL GMBH; and SANDOZ GMBH;	)	**FINAL PRE-TRIAL ORDER**
Defendants.	)	

PUBLIC REDACTED VERSION

This matter having come before the Court for a pretrial conference pursuant to Fed. R. Civ. P. 16; and the undersigned counsel listed below from Walsh Pizzi O'Reilly Falanga LLP and Sidley Austin LLP having appeared for Plaintiffs Immunex Corp. ("Immunex") and Amgen Manufacturing, Ltd. ("AML"), the undersigned counsel listed below from Gibbons P.C. and Williams & Connolly LLP having appeared for Plaintiff Hoffmann-La Roche Inc. ("Roche"), and the undersigned counsel from Hill Wallack LLP and Winston & Strawn LLP having appeared for Defendants Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH (collectively "Sandoz" or "Defendants"), and counsel having been notified that a bench trial in these matters has been scheduled before the Hon. Claire C. Cecchi beginning on September 11, 2018 at 9:30 a.m., the following Final Pretrial Order is hereby entered:

I. JURISDICTION

This is a patent infringement matter arising under the Patent Laws of the United States, Title 35, United States Code. For purposes of this action only, no party has contested that this Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and

1338(a).[1] For the purposes of this action only, no party has contested personal jurisdiction or venue under 28 U.S.C. §§ 1391(b), (c) or 1400(b).

II. OVERVIEW OF THE CASE

On July 30, 2015, Sandoz submitted a Biologics License Application ("abbreviated BLA" or "aBLA") pursuant to 42 U.S.C. § 262(k) of the Biologics Price Competition and Innovation Act ("the BPCIA")[2] (*i.e.*, a section 351(k) application) seeking authorization from the Food and Drug Administration ("FDA") to market Erelzi®, a biosimilar of Immunex's ENBREL® (etanercept) product ("Defendants' Biosimilar Etanercept"). On September 29, 2015, the FDA accepted for review Sandoz's aBLA.

On December 18, 2015, Immunex provided Sandoz with a list of patents for which Immunex believed that a claim of infringement could be reasonably asserted based on Defendants' Biosimilar Etanercept. *See* 42 U.S.C. § 262(*l*)(3)(A). The list of patents included United States Patent Nos. 8,063,182 ("the '182 patent"), 8,163,522 ("the '522 patent") (collectively referred to as the "Patents-in-Suit"). Plaintiffs' list also included U.S. Patent Nos. 7,915,225 ("the Finck '225 patent"), 8,119,605 ("the Finck '605 patent"), and 8,722,631 ("the Finck '631 patent") (collectively, "the Finck Patents").[3]

A. Plaintiffs' Allegations and Request for Relief

Immunex/AML and Roche (collectively "Plaintiffs") allege that Sandoz's submission of an aBLA referencing Immunex's ENBREL® product is an act of infringement under 35 U.S.C. §

[1] Plaintiffs further assert that the Court has subject matter jurisdiction pursuant to § 2201(a). Defendants disagree.

[2] 42 U.S.C. § 262(k) of the BPCIA is also known as § 351(k) of the Public Health Service Act ("PHSA").

[3] [redacted]

271(e)(2)(C). Specifically, Plaintiffs allege that Sandoz has infringed claims 11-12 and 35-36 of the '182 patent and claims 3, 8, and 10 of the '522 patent (the "Asserted Claims").

Plaintiffs also allege that the commercial manufacture, use, sale, offer for sale, and/or importation of Defendants' Biosimilar Etanercept into the United States will infringe the Asserted Claims of the '182 patent under 35 U.S.C. § 271(a) and the Asserted Claims of the '522 patent under 35 U.S.C. § 271(g).

Plaintiffs request that the Court enter judgment that Defendants have infringed each and every one of the Asserted Claims of each of the Patents-in-Suit, and that the Asserted Claims of Patents-in-Suit are not invalid.

Plaintiffs further request that the Court enter an order enjoining Defendants, as well as all of Defendants' officers, employees, agents, representatives, affiliates, assignees, and successors, and all persons acting on behalf or at the direction of, or in concert with Defendants, from engaging in the manufacture, use, sale, offer for sale, and/or importation into the United States of Defendants' Biosimilar Etanercept or any other product that would infringe the Asserted Claims of the '182 patent or, by its making, infringe the Asserted Claims of the '522 patent, prior to the respective expiration date of each of the Patents-in-Suit.

Plaintiffs further request that the Court declare that this is an exceptional case pursuant to 35 U.S.C. § 285 and award Plaintiffs their reasonable attorneys' fees and costs incurred in this action and/or any further relief as deemed just and proper by this Court.

B. Defendants' Defenses, Allegations, and Request for Relief

This patent infringement action arises under 35 U.S.C. § 271, including 35 U.S.C. § 271(e)(2)(C), which was enacted in 2010 as part of the BPCIA. The BPCIA established, *inter alia*, an abbreviated pathway (a § 351(k) application) for regulatory approval of follow-on

biological products that are "highly similar" to a previously approved biological drug product ("reference product").

Defendants allege that the Asserted Claims are invalid under the judicially created doctrine of obviousness-type double patenting; for obviousness under 35 U.S.C. § 103; and/or for lack of written description and enablement under 35 U.S.C. § 112.[4] Defendants allege that asserted claims 35 and 36 of the '182 patent are also invalid for anticipation under 35 U.S.C. § 102.

Defendants do not contest infringement of any valid and enforceable Asserted Claim of the '182 patent.[5] Defendants do not contest infringement of any valid and enforceable Asserted Claim of the '522 patent, under the Court's August 20, 2018 claim construction ruling, without prejudice to Defendants' right to appeal that ruling.

Defendants request that the Court enter judgment that each of the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting, obviousness, inadequate written description, and/or lack of enablement. Defendants also request that the Court enter judgment that claims 35 and 36 of the '182 patent are invalid for anticipation.

Defendants further request that the Court declare that this is an exceptional case pursuant to 35 U.S.C. § 285 and award Defendants their reasonable attorneys' fees and costs incurred in this action and/or any further relief as deemed just and proper by this Court.

III. PENDING/CONTEMPLATED MOTIONS/TRIAL BRIEFS

The following motions/issues are presently pending before the Court:

[4] Unless otherwise indicated, all citations to Title 35, United States Code, Section 102, Section 103, Section 112, and Section 135, are to the pre-America Invents Act ("pre-AIA") version of the Patent Act.

[5] February 21, 2018 letter from Eric I. Abraham to Liza M. Walsh; *see also* May 15, 2018 Joint Pretrial Report to Judge Cecchi, D.I. 486 ("Joint Pretrial Report").

1. The parties dispute the meaning of the word "hinge" in the phrase "-hinge-CH2-CH3 region of a human [IgG/IgG1]." D.I. 513; D.I 529; D.I. 541. The Court ruled that this is an issue to be determined at trial. D.I. 572.

2. Defendants have filed the following motion *in limine*: Motion in *Limine* Regarding Priority Date of Claims 35 and 36 of the '182 Patent, D.I. 518; D.I. 531; D.I. 538.[6]

3. On August 15, 2018, the Court denied or administratively terminated Plaintiffs' pending Motions *in Limine* and denied or administratively terminated Defendants' pending Motions *in Limine* and *Daubert* motions. D.I. 572.

Pretrial briefs will be filed with the Court by each side on August 27, 2018 by 5:00 P.M. EDT (D.I. 600), with Plaintiffs collectively submitting one brief, and Defendants collectively submitting one brief. Briefs shall be limited to 45 pages per side (if 12 point font) or 60 pages per side (if 14 point font).

IV. STIPULATION OF FACTS

A. The Parties

1. Plaintiff Immunex Corporation ("Immunex") is a corporation organized and existing under the laws of the State of Washington with its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320. Amgen Inc. acquired Immunex in July 2002. Immunex is a wholly-owned subsidiary of Amgen Inc.

2. Plaintiff Amgen Manufacturing, Limited ("AML") is a corporation existing under the laws of the Territory of Bermuda, with its principal place of business at Road 31 km 24.6, Juncos, Puerto Rico 00777. AML is a wholly-owned subsidiary of Amgen Inc.

[6] Defendants have agreed to hold in abeyance this motion. *See* Transcript of Hearing Before the Hon. Claire C. Cecchi, June 29, 2018, at 101:20-22 ("June 29, 2018 Hearing Transcript"). The Court administratively terminated this motion on August 16, 2018. D.I. 572 at 15.

3. Plaintiff Hoffmann-La Roche Inc. ("Roche") is a corporation organized and existing under the laws of the State of New Jersey with its principal place of business at 150 Clove Road, Suite 8, Little Falls, New Jersey 07424.

4. Defendant Sandoz Inc. is a corporation organized and existing under the laws of the State of Colorado, with its principal place of business at 100 College Road West, Princeton, New Jersey 08540.

5. Defendant Sandoz International GmbH is a Gesellschaft mit beschränkter Haftung (Company with Limited Liability) existing under the laws of the Federal Republic of Germany with its principal place of business at Industriestraße 25, 83607 Holzkirchen, Germany.

6. Defendant Sandoz GmbH is a Gesellschaft mit beschränkter Haftung (Company with Limited Liability) existing under the laws of the Republic of Austria with its principal place of business at Biochemiestraße 10, 6250 Kundl, Austria.

B. The Patents-in-Suit

1. The '182 Patent

7. The '182 patent is titled "Human TNF Receptor Fusion Protein," and issued on November 22, 2011. The named inventors listed on the face of the '182 patent are Manfred Brockhaus, Reiner Gentz, Zlatko Dembic, Werner Lesslauer, Hansruedi Loetscher, and Ernst-Jurgen Schlaeger. Each of the named inventors of the '182 patent was formerly an employee of a corporate affiliate of Plaintiff Roche.

8. Plaintiff Roche is identified as the assignee on the face of the '182 patent.

9. The '182 patent issued from U.S. Patent Application No. 08/444,790 ("the Brockhaus '790 application"). The Brockhaus '790 application was filed on May 19, 1995 as a division of U.S. Patent Application No. 08/095,640 ("the Brockhaus '640 application"), which issued as U.S. Patent No. 5,610,279 ("the Brockhaus '279 patent") on March 11, 1997. The '640

application was filed on July 21, 1993 as a continuation of U.S. Patent Application No. 07/580,013 ("the Brockhaus '013 application").

10. On its face, the '182 patent also claims priority to four foreign patent applications: (i) Swiss Patent Application No. 3319/89, filed on September 12, 1989; (ii) Swiss Patent Application No. 746/90, filed on March 8, 1990; (iii) Swiss Patent Application No. 1347/90, filed on April 20, 1990; and (iv) European Patent Application No. 90116707 ("the Brockhaus '707 application"), filed on August 31, 1990.

11. The '182 patent issued on November 22, 2011.

12. The '182 patent expires on November 22, 2028.

13. Plaintiffs assert infringement of claims 11-12 and 35-36 of the '182 patent.

14. Claim 1 of the '182 patent is not asserted, but is the independent claim on which Asserted Claims 11-12 depend.

15. Claim 1 of the '182 patent recites: "A protein comprising: (a) a human tumor necrosis factor (TNF)-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor (i) specifically binds human TNF, (ii) has an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, and (iii) comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10); and (b) all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region; wherein said protein specifically binds human TNF."

16. Claim 11 of the '182 patent recites: "The protein of claim 1, wherein the protein consists essentially of the extracellular region of the insoluble human TNF receptor and all the domains of the constant region of a human IgG_1 immunoglobulin heavy chain other than the first domain of the constant region."

17. Claim 12 of the '182 patent recites: "A pharmaceutical composition comprising the protein of claim 11 and a pharmaceutically acceptable carrier material."

18. Claim 30 of the '182 patent is not asserted, but is the independent claim on which Asserted Claims 35-36 depend.

19. Claim 30 of the '182 patent recites: "A protein comprising (a) human tumor necrosis factor (TNF) binding soluble fragment of the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC on Oct. 17, 2006 under accession number PTA 7942, (b) all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region; wherein said protein specifically binds human TNF."

20. Claim 35 of the '182 patent recites: "The protein of claim 30, wherein the protein consists essentially of the extracellular region of the human tumor necrosis factor (TNF) receptor amino acid sequence encoded by the cDNA insert, and all the domains of the constant region of a human IgG_1 immunoglobulin heavy chain other than the first domain of the constant region."

21. Claim 36 of the '182 patent recites: "A pharmaceutical composition comprising the protein of claim 35 and a pharmaceutically acceptable carrier material."

2. The '522 Patent

22. The '522 patent is titled "Human TNF Receptor," and issued on April 24, 2012. The named inventors listed on the face of the '522 patent are Manfred Brockhaus, Reiner Gentz, Zlatko Dembic, Werner Lesslauer, Hansruedi Loetscher, and Ernst-Jurgen Schlaeger. Each of the named inventors of the '522 patent was formerly an employee of a corporate affiliate of Plaintiff Roche.

23. Plaintiff Roche is identified as the assignee on the face of the '522 patent.

24. The '522 patent issued from U.S. Patent Application No. 08/444,791 ("the Brockhaus '791 application"). The Brockhaus '791 application was filed on May 19, 1995 as a division of the Brockhaus '640 application, which issued as the Brockhaus '279 patent on March 11, 1997. The Brockhaus '640 application was filed on July 21, 1993 as a continuation of the Brockhaus '013 application.

25. On its face, the '522 patent also claims priority to four foreign patent applications: (i) Swiss Patent Application No. 3319/89, filed on September 12, 1989; (ii) Swiss Patent Application No. 746/90, filed on March 8, 1990; (iii) Swiss Patent Application No. 1347/90, filed on April 20, 1990; and (iv) European Patent Application No. 90116707 ("the Brockhaus '707 application"), filed on August 31, 1990.

26. The '522 patent issued on April 24, 2012.

27. The '522 patent expires on April 24, 2029.

28. Plaintiffs assert claims 3, 8, and 10 of the '522 patent.

29. Claim 1 of the '522 patent is not asserted, but is the independent claim on which Asserted Claim 3 depends.

30. Claim 1 of the '522 patent recites: "A method comprising the steps of: (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes a protein consisting of: (i) the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel and comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and (ii) all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region,

and (b) purifying an expression product of the polynucleotide from the cell mass or the culture medium."

31. Claim 3 of the '522 patent recites: "The method of claim 1, wherein the IgG heavy chain is an IgG_1 heavy chain."

32. Claim 7 of the '522 patent is not asserted, but is the independent claim on which Asserted Claims 8 and 10 depend.

33. Claim 7 of the '522 patent recites: "A method comprising the steps of: (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes a protein consisting of: (i) the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor comprises the amino acid sequence of SEQ ID NO:27 and (ii) all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region, and (b) purifying an expression product of the polynucleotide from the cell mass or the culture medium."

34. Claim 8 of the '522 patent recites: "The method of claim 7, wherein the human IgG immunoglobulin heavy chain is an IgG_1 heavy chain."

35. Claim 10 of the '522 patent recites: "The method of claim 8, wherein the host cell is a CHO cell."

C. Etanercept

1. ENBREL®

36. Immunex is the reference product sponsor of the biological drug product ENBREL® in the United States. The active ingredient in ENBREL® is etanercept.

37. The etanercept drug substance in ENBREL® is a dimeric fusion protein consisting of the extracellular region of the p75 TNF receptor fused to hinge-CH2-CH3 region of a human IgG1. The amino acid sequence of etanercept is identified as Sequence A in **Joint Exhibit 1**.

38. ENBREL® (etanercept) is presently approved by FDA for the following indications: rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and plaque psoriasis (PsO).

39. Immunex filed Biologic License Application ("BLA") No. 103795 seeking FDA approval of ENBREL® (etanercept). FDA approved BLA No. 103795 on November 2, 1998 for use of ENBREL® (etanercept) in the treatment of rheumatoid arthritis. Immunex holds the rights to BLA No. 103795.

40. Immunex filed supplements to BLA No. 103795, requesting that ENBREL® (etanercept) be approved for certain additional indications. FDA approved ENBREL® (etanercept) for the treatment of polyarticular juvenile idiopathic arthritis (JIA) in 1999, psoriatic arthritis (PsA) in 2002, ankylosing spondylitis (AS) in 2003, and plaque psoriasis (PsO) in 2004.

2. Erelzi®, Defendants' Biosimilar Etanercept

41. On July 30, 2015, Sandoz Inc. submitted a Section 351(k) application, aBLA No. 761042, to FDA, seeking authorization to market Erelzi® as a biosimilar version of Immunex's ENBREL® (etanercept) product in the United States.

42. On September 29, 2015, FDA accepted for review Sandoz's aBLA No. 761042.

43. On August 30, 2016, FDA approved Defendants' Biosimilar Etanercept for all the indications in which ENBREL® (etanercept) had been approved at that time: rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and plaque psoriasis (PsO).

44. On July 27, 2017, Sandoz filed an amendment to its aBLA No. 761042 seeking FDA approval for a new proposed label for Erelzi® that removed the indications for psoriatic arthritis (PsA) and plaque psoriasis (PsO). The amendment was made because these indications remain protected by the Finck Patents until August 13, 2019.

45. On January 26, 2018, FDA approved the new label for Erelzi®. The new label for Erelzi® states that it is indicated for the treatment of rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (JIA), and ankylosing spondylitis (AS). Erelzi® is not indicated for the treatment of psoriatic arthritis (PsA) or plaque psoriasis (PsO).

46. The etanercept drug substance in Defendants' Biosimilar Etanercept is a dimeric fusion protein consisting of the extracellular region of the p75 TNF receptor fused to hinge-CH2-CH3 region of a human IgG1. The etanercept drug substance in Defendants' Biosimilar Etanercept has the amino acid sequence identified as Sequence A in **Joint Exhibit 1**, which is the same amino acid sequence as the etanercept drug substance in Immunex's ENBREL® biological drug product.

D. The Litigation

47. On February 26, 2016, Plaintiffs filed a Complaint against Defendants asserting infringement under 35 U.S.C. § 271(e)(2)(C), seeking a declaratory judgment of infringement under, 35 U.S.C. §§ 271(a), (b), (g), and further seeking, among other things, damages or other monetary relief adequate to compensate Plaintiffs for Defendants' infringement, an injunction preventing infringement and future infringement until the later of the expiration dates of the Patents-in-Suit, a declaration that this is an exceptional case such that Plaintiffs should be awarded attorneys' fees and costs pursuant to 35 U.S.C. § 285, and such other relief as the Court may deem just and proper. D.I. 1.

48. On March 21, 2016, Sandoz Inc. filed its Answer denying infringement of, *inter alia*, the Patents-in-Suit. Sandoz Inc. also denied that Plaintiffs are entitled to any relief sought in the Complaint, and denied that the case is exceptional. Sandoz Inc. also pled its affirmative defenses that the Patents-in-Suit are invalid for failing to satisfy one or more sections of Title 35 of the United States Code, invalid under the judicially created doctrine of obviousness-type

double patenting, and/or unenforceable due to prosecution laches. Sandoz Inc. requested that: (a) Plaintiffs' complaint be dismissed with prejudice and judgment be entered in favor of Sandoz Inc.; (b) a declaration that this case is exceptional under 35 U.S.C. § 285 entitling Sandoz Inc. to relief under that statute; and (c) an award of such other and further relief to Sandoz Inc. that the Court deems just and proper. D.I. 28.

49. On September 20, 2016, Sandoz International GmbH filed its Answer denying infringement of, *inter alia*, the Patents-in-Suit. Sandoz International GmbH also denied that Plaintiffs are entitled to any relief sought in the Complaint, and denied that the case is exceptional. Sandoz International GmbH also pled its affirmative defenses that the Patents-in-Suit and the Finck Patents are invalid for failing to satisfy one or more sections of Title 35 of the United States Code, invalid under the judicially created doctrine of obviousness-type double patenting, and/or unenforceable due to prosecution laches. Sandoz International GmbH requested that: (a) Plaintiffs' complaint be dismissed with prejudice and judgment be entered in favor of Sandoz International GmbH; (b) a declaration that this case is exceptional under 35 U.S.C. § 285 entitling Sandoz International GmbH to relief under that statute; and (c) an award of such other and further relief to Sandoz International GmbH that the Court deems just and proper. D.I. 105.

50. On October 27, 2016 Sandoz GmbH filed its Answer denying infringement of, *inter alia*, the Patents-in-Suit. Sandoz GmbH also denied that Plaintiffs are entitled to any relief sought in the Complaint, and denied that the case is exceptional. Sandoz GmbH also pled its affirmative defenses that the Patents-in-Suit and the Finck Patents are invalid for failing to satisfy one or more sections of Title 35 of the United States Code, invalid under the judicially created doctrine of obviousness-type double patenting, and/or unenforceable due to prosecution

laches. Sandoz GmbH requested that: (a) Plaintiffs' complaint be dismissed with prejudice and judgment be entered in favor of Sandoz GmbH; (b) a declaration that this case is exceptional under 35 U.S.C. § 285 entitling Sandoz GmbH to relief under that statute; and (c) an award of such other and further relief to Sandoz GmbH that the Court deems just and proper. D.I. 121.

V. STIPULATIONS AND CONSENT ORDERS

51. On August 11, 2016, the Court entered a Consent Preliminary Injunction pursuant to Fed. R. Civ. P. 65(d), subject to the terms and conditions of a sealed Stipulation. D.I. 95.

52. On July 11, 2017, Defendants withdrew their prosecution laches defense against the Patents-in-Suit. Defendants informed the Court of their withdrawal of this defense during the July 13, 2017 status conference with the Court. D.I. 199.

53. On October 20, 2017, the Court entered a Consent Order regarding constructive amendment of Defendants' invalidity contentions and case schedule. D.I. 253.

54. On November 3, 2017, Plaintiffs withdrew their claims of infringement of claims 1-10 and 13-34 of the '182 patent and elected to assert at trial claims 11, 12, 35 and 36 of the '182 patent and claims 1-3 and 7-10 of the '522 patent. Plaintiffs informed the Court of the same in a letter to the Court filed under seal on November 3, 2017. D.I. 268.

55. On January 26, 2018, the Court entered a Stipulation and Order regarding Plaintiffs' motion to strike portions of the Rebuttal Expert Report of Daniel Capon, Ph.D. D.I. 367.

56. In the May 15, 2018 Joint Pretrial Report, Plaintiffs identified that they are asserting at trial infringement of claims 11, 12, 35, and 36 of the '182 patent and claims 1-3 and 7-10 of the '522 patent.[7] D.I. 486 at 6.

57. In the May 15, 2018 Joint Pretrial Report, Defendants indicated they do not contest that Defendants' Biosimilar Etanercept infringes the Asserted Claims of the '182 patent. D.I. 486 at 6.

58. In the Joint Pretrial Report, Defendants listed the following defenses: (a) non-infringement of the Asserted Claims of the '522 patent and (b) three theories of invalidity:

- Obviousness based on one or more of six purported prior art combinations;
- Obviousness-type double patenting based on one or more of three purported reference families; and
- Lack of written description and enablement. D.I. 486 at 6-7.

59. At the June 29, 2018 hearing, the Court confirmed that Defendants may assert that claims 35 and 36 of the '182 patent are anticipated.[8]

60. On June 7, 2018, the Court entered an Amended Consent Preliminary Injunction pursuant to Fed. R. Civ. P. 65(d), subject to the terms and conditions of a sealed Amended Stipulation. D.I. 509. [redacted]

[7] On August 13, 2018, Plaintiffs identified that they are asserting at trial only claims 11-12 and 35-36 of the '182 patent, and claims 3, 8, and 10 of the '522 patent.

[8] June 29, 2018 Hearing Transcript at 107:11-23.

61. Sandoz agreed to hold in abeyance its Motion in *Limine* Regarding the Priority Date of Claims 35 and 36 of the '182 Patent. D.I. 518.[9]

62. On August 21, 2018, the Court entered an Order to Preclude Introduction of Arguments on Defenses and Issues No Longer in the Case. D.I. 516, 597.

63. On August 22, 2018, the Court resolved the parties' dispute regarding the construction of the term "wherein the polynucleotide contains the genetic information for a protein consisting of," relevant to the Asserted Claims of the '522 patent. D.I. 596. Specifically, the Court construed the term to mean "wherein the polynucleotide contains the genetic information for a protein consisting of." *Id.* Based on the Court's claim construction, and without prejudice to their right to appeal the Court's claim construction ruling, Defendants confirmed that they will not contest infringement of the Asserted Claims of the '522 patent at trial.

64. On September 10, 2018, Defendants stipulated that the Sandoz's submission aBLA 761042 infringed the Asserted Claims of the Patents-in-Suit under 35 U.S.C. § 271(e)(2)(C). Defendants also stipulated that Defendants' making, using, offering to sell, or selling of Defendants' Biosimilar Etanercept within the United States, or Defendants' importation of Defendants' Biosimilar Etanercept into the United States, will infringe claims 11-12 and 35-36 of the '182 under 35 U.S.C. § 271(a); and Defendants' making, using, offering to sell, or selling of Defendants' Biosimilar Etanercept within the United States, or Defendants' importation of Defendants' Biosimilar Etanercept into the United States, will infringe claims 3, 8, and 10 of the '522 patent under 35 U.S.C. § 271(g).

[9] The Court administratively terminated this motion on August 16, 2018. D.I. 572 at 15.

65. On September 10, 2018, Defendants agreed to Plaintiffs' proposed construction of the following term of the '182 Patent: "all of the domains of the constant region of a human immunoglobulin IgG[1] heavy chain other than the first domain of said constant region" and the following term of the '522 Patent: "all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region." (D.I. 618).

VI. CLAIM CONSTRUCTIONS

66. The parties have agreed upon the proper construction of the following claim terms from the '182 patent and the '522 patent, and the Court has entered orders on the construction of these claims terms (D.I. 136, D.I. 144):

Term	Relevant Claims	Agreed Construction
"the extracellular region of the insoluble human TNF receptor" "the extracellular region of the human tumor necrosis factor (TNF) receptor"	Asserted Claim 11 of the '182 patent Asserted Claim 12 of the '182 patent (by dependence on Asserted Claim 11) Asserted Claim 35 of the '182 patent Asserted Claim 36 of the '182 patent (by dependence on Asserted Claim 35)	Plain and ordinary meaning: "that portion of the human TNF receptor that protrudes outside the cell"[10]
"the extracellular region of the human tumor necrosis factor (TNF) receptor, wherein the insoluble human TNF receptor has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS polyacrylamide gel and comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10)" "the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor comprises the amino acid sequence of SEQ ID NO: 27"	Asserted Claim 3 of the '522 patent (by dependence on Claim 1) Asserted Claims 8 and 10 of the '522 Patent (by dependence on Claim 7)	Plain and ordinary meaning: "that portion of the human 75 kDa TNF receptor that protrudes outside the cell"[11]

[10] D.I. 136.

[11] D.I. 136.

Term	Relevant Claims	Agreed Construction
"all of the domains of the constant region of a human immunoglobulin IgG[1] heavy chain other than the first domain of said constant region"	Claims 1 and 30 of the '182 patent (unasserted, but the independent claims from which Asserted Claims 11-12 and 35-36 respectively depend) Asserted Claims 11 and 35 of the '182 patent (expressly and by dependence on unasserted claims 1 and 30, respectively) Asserted Claims 12 and 36 of the '182 patent (by dependence on Asserted Claims 11 and 35, respectively)	Plain and ordinary meaning: "'-hinge-CH2-CH3' region of a human [IgG/IgG1]"[12]
"all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region"	Asserted Claims 3, 8, and 10 of the '522 patent (by dependence on Claims 1 and 7)	
"specifically binds human TNF"	Claims 1 and 30 of the '182 patent (unasserted, but the independent claims from which Asserted Claims 11-12 and 35-36 respectively depend) Asserted Claims 11-12 and 35-36 of the '182 patent (by dependence on Asserted Claims 1 and 30, respectively)	Plain and ordinary meaning: "has the ability to strongly and stably bind human TNF"[13]

[12] D.I. 144. The plain and ordinary meaning of "hinge" is disputed. The Court has indicated that "both sides will be permitted to offer expert testimony as to how a POSA as of August 1990 would have understood the meaning of 'hinge.'" D.I. 572 at 9. The Court has further noted that "if additional construction is needed to determine the scope of the claims, the Court will do so after further development of the record. *Id.*, footnote 4.

[13] D.I. 144.

67. The Court has entered an order construing the following claim term of the '522 patent that had been disputed by the parties (D.I. 596):

Term	Relevant Claims	Court's Construction
"wherein the polynucleotide encodes a protein consisting of"	Asserted Claims 3, 8, and 10 of the '522 patent	"wherein the polynucleotide contains the genetic information for a protein consisting of"

68. The parties have agreed upon the construction of the following claim term (D.I. 618):

Claim Terms	Construction
'182 Patent: "all of the domains of the constant region of a human immunoglobulin IgG[1] heavy chain other than the first domain of said constant region" '522 Patent: "all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region"	"***the exon-encoded*** '-hinge-CH2-CH3' region of a human [IgG/IgG1]"

69. **Plaintiffs' Exhibit 1** shows Plaintiffs' version of the language of the Asserted Claims (including claims from which the Asserted Claims depend) as the Asserted Claims would be understood through the undisputed, plain-and-ordinary-meaning claim constructions.

70. Defendants object to **Plaintiffs' Exhibit 1** as mischaracterizing how the Asserted Claims would be understood through the undisputed, plain-and-ordinary-meaning claim constructions. Plaintiffs paraphrase certain portions of the claims to give the claims an alternative meaning, rather than merely substituting the disputed claim terms with the agreed-

upon constructions. The claims are best understood through the presentation of evidence during trial.

VII. ISSUES TO BE LITIGATED[14]

71.

A. Infringement (35 U.S.C. §§ 271(a), (e)(2)(C) and (g))

1. Plaintiffs' Statement

72. Under 35 U.S.C. § 271(e)(2)(C), the submission of an application seeking approval of a biological product is an act of infringement with respect to a patent that is identified in the list of patents described in section 351(*l*)(3) of the PHSA (including as provided under section 351(*l*)(7) of such Act). *See Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1670 (2017).

73. Defendants do not contest that Defendants' Biosimilar Etanercept meets each and every limitation of each of the Asserted Claims of the '182 patent and therefore infringes the Asserted Claims of the '182 patent under 35 U.S.C § 271(a) and (e)(2)(C).

74. Defendants do also not contest that their method of making of Defendants' Biosimilar Etanercept meets each and every limitation of each of the Asserted Claims of the '522 patent and therefore infringes the Asserted Claims of the '522 patent under 35 U.S.C § 271(g) and (e)(2)(C).

75. Defendants therefore do not contest that the commercial manufacture, use, sale, offer for sale, and/or importation of Defendants' Biosimilar Etanercept into the United States

[14] The parties provide the following summary of the issues in the case without waiver of their rights to present their claims and defenses with more specificity during trial.

will infringe the Asserted Claims of the '182 patent under 35 U.S.C. § 271(a) and the Asserted Claims of the '522 patent under 35 U.S.C. § 271(g) and that the submission of Defendants' Section 351(k) application, aBLA No. 761042, to FDA, seeking authorization to market Erelzi® as a biosimilar version of Immunex's ENBREL® (etanercept) product in the United States is an act of infringement under 35 U.S.C. § 271(e)(2)(C).

2. Defendants' Statement

76. Defendants dispute that there are any remaining issues to be litigated at trial relating to infringement, without prejudice to Defendants' right to appeal. Plaintiffs mischaracterize the issues not contested by Defendants.

77. As stated in the May 15, 2018 Joint Pretrial Report, Defendants do not contest that the Asserted Claims of the '182 patent cover Defendants' Biosimilar Etanercept, but do not thereby waive any argument that the specification fails to adequately describe or enable the Asserted Claims.

78. Defendants do not contest infringement of the '522 patent, under the Court's claim construction (D.I. 595), without prejudice to their right to appeal the Court's claim construction ruling.

79. The submission of Defendants' Section 351(k) application pursuant to the BPCIA, aBLA No. 761042, to FDA, seeking authorization to market Erelzi® as a biosimilar version of Immunex's ENBREL® (etanercept) product in the United States does not give rise to liability for patent infringement. The Supreme Court has explained that the BPCIA "enables the parties to bring infringement actions at certain points in the application process, even *if the applicant has not yet committed an act that would traditionally constitute patent infringement.*" *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1669 (2017) (emphasis added). The Supreme Court "refer[s] to this kind of preapproval infringement as 'artificial' infringement." *Id.*

80. Defendants' activities in the United States thus far have not infringed any Asserted Claim of the Patents-in-Suit under 35 U.S.C. §§ 271(a) or (g). 35 U.S.C. § 271(e)(1) provides a safe harbor for any acts of infringement "solely for uses reasonably related to the development or submission of any information" to the FDA, which regulates the manufacture, use and sale of drugs—such as Defendants' Biosimilar Etanercept.

B. Obviousness-Type Double Patenting

1. Defendants' Statement

81. "[I]t is a bedrock principle of our patent system that when a patent expires, the public is free to use not only the same invention claimed in the expired patent but also obvious or patentably indistinct modifications of that invention. . . . The double patenting doctrine has always been implemented to effectively uphold that principle." *Gilead Sci., Inc. v. Natco Pharma Ltd.*, 753 F.3d 1208, 1214 (Fed. Cir. 2014); *see also Boehringer Ingelheim Int'l GmbH v. Barr Labs., Inc.*, 592 F.3d 1340, 1347 (Fed. Cir. 2010).

82. "Generally, an obviousness-type double patenting analysis entails two steps. First, as a matter of law, a court construes the claim in the earlier patent and the claim in the later patent and determines the differences. . . . Second, the court determines whether the differences in subject matter between the two claims render the claims patentably distinct." *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001). "A later claim that is not patentably distinct from an earlier claim in a commonly owned patent is invalid for obvious-type double patenting. . . . A later patent claim is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim." *Id.*

83. "As a general rule, a 'one-way' test applies to determine obviousness-type double patenting." *In re Hubbell*, 709 F.3d 1140, 1149 (Fed. Cir. 2013). The two-way test is "a narrow exception to the general rule of the one-way test," which "is appropriate only in the 'unusual

circumstance' where 'the PTO is solely responsible for the delay in causing the second-filed application to issue prior to the first.'" *Id.* Application of the two-way test requires circumstances where both "(1) a second-filed application issues prior to a first-filed application, and (2) 'the PTO is solely responsible for the delay' in the issuance of the first-filed application." *In re Janssen Biotech, Inc.*, 880 F.3d 1315, 1325 (Fed. Cir. 2018). The Federal Circuit has declined to apply the two-way test where an applicant "had significant control over the rate of prosecution of the application" and has not limited the analysis to the time period during which both applications where pending. *In re Emert*, 124 F.3d at 1498 (Fed. Cir. 1997).

84. "There are two justifications for obviousness-type double patenting. The first is 'to prevent unjustified timewise extension of the right to exclude granted by a patent no matter how the extension is brought about.' The second rationale is to prevent multiple infringement suits by different assignees asserting essentially the same patented invention." *Hubbell*, 709 F.3d at 1145. Thus, an earlier-expiring patent that either has one or more inventors in common with a later-expiring patent or shares a common assignee or owner with the later-expiring patent may be used as an obviousness-type double patenting reference. *Id.* at 1146 (affirming that "obviousness-type double patenting applies where an application and a conflicting patent have one or more inventors in common but the inventive entities are not identical and the applications were never commonly owned"); *In re Longi*, 759 F.2d 887, 895 (Fed. Cir. 1985) ("[W]e hold that double patenting of the obviousness type, as applied to commonly-owned applications made by different inventive entities, is still a viable doctrine.").

85. To guard against the potential for multiple infringement suits by different entities asserting the same patented invention, the Federal Circuit identifies the entity that has "all substantial rights" to the patent as the owner who has the authority to enforce the patent.

Namely, "a party that has been granted all substantial rights under the patent is considered the owner regardless of how the parties characterize the transaction that conveyed those rights." *Speedplay, Inc. v. Bebop, Inc.*, 211 F.3d 1245, 1250 (Fed. Cir. 2000); *see also Diamond Coating Techs., LLC v. Hyndai Motor Am.*, 823 F.3d 615, 618-19 (Fed. Cir. 2016). Common ownership for purposes of obviousness-type double patenting may be established at any point in time, including after the time of invention. *See Geneva Pharm., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1377, 1382-86 (Fed. Cir. 2003) (holding patents invalid for obviousness-type double patenting where the patentee "own[ed] the [reference] patents because [it] has merged with the original assignees of those patents"); *cf. STC.UNM v. Intel Corp.*, 754 F.3d 940, 944 (Fed. Cir. 2014) (affirming district court's dismissal for lack of standing where plaintiff assigned an interest in the patent-in-suit to third-party during litigation to establish co-ownership of reference patent under terms of terminal disclaimer filed during prosecution to overcome double patenting rejection, but where co-owner then refused to join litigation). *See also In re Hubbell*, 709 F.3d 1140, 1145 (Fed. Cir. 2013) (obviousness type double patenting serves "to prevent unjustified timewise extension of the right to exclude granted by a patent no matter how the extension is brought about").

86. Section 121 may provide a safe harbor from double patenting invalidation for certain "patent[s] issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement." 35 U.S.C. § 121. The PTO may issue a restriction requirement "when 'independent and distinct inventions' are claimed in one application." *Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 687 (Fed. Cir. 1990) (quoting 35 U.S.C. § 121). The § 121 safe harbor "applies only to the divisional applications that are 'filed as a result of' a restriction requirement. Plain

common sense dictates that a divisional application filed as a result of a restriction requirement may not contain claims drawn to the invention set forth in the claims elected and prosecuted to patent in the parent application. The divisional application must have claims drawn only to the 'other invention.'" *Id.* at 687.

87. The claims of the divisional application must maintain "consonance" with the divisions imposed by the PTO's restriction requirement. Specifically, "the line of demarcation between the 'independent and distinct inventions' that prompted the restriction requirement be maintained. Though the claims may be amended, they must not be so amended as to bring them back over the line imposed in the restriction requirement. Where that line is crossed the prohibition of the third sentence of Section 121 does not apply." *Id.* at 688.

a. Defendants' Statement of the Issues of Law to be Litigated

(i) Obviousness-Type Double Patenting Over the Finck '225, '605, and '631 Patents

88. Whether each of the Finck '225 patent, the Finck '605 patent, and the Finck '631 patent are available as obviousness-type double patenting references to invalidate the Patents-in-Suit?

89. Whether a reference patent and a challenged patent are deemed "commonly owned" for purposes of obviousness-type double patenting, when the owner of the reference patent acquires all substantial rights to the challenged patent after the date of invention?

90. Whether a later-filed but earlier-expiring patent is available as an obviousness-type double patenting reference to invalidate an earlier-filed but later-expiring challenged patent, when the later-filed patent expires earlier than the earlier-filed challenged patent due to the changes in the grant of U.S. patent term implemented by the Uruguay Round Agreements Act of the General Agreement on Tariffs and Trade (GATT)?

91. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting over each of claim 1 of the Finck '225 patent, claim 1 of the Finck '605 patent, or claim 1 of the Finck '631 patent under the one-way test?

92. Whether Plaintiffs have shown that the Court should apply the two-way test, instead of the presumptive one-way test, for the Finck '225 patent, the Finck '605 patent, and the Finck '631 patent as obviousness-type double patenting references to the Patents-in-Suit?

(ii) Obviousness-Type Double Patenting Over the Jacobs '690 Patent

93. Whether the Jacobs '690 patent is available as an obviousness-type double patenting reference to invalidate the Patents-in-Suit?

94. Whether a reference patent and a challenged patent are deemed "commonly owned" for purposes of obviousness-type double patenting, when the owner of the reference patent acquires all substantial rights to the challenged patent after the date of invention?

95. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting over claim 3 of the Jacobs '690 patent under the one-way test?

96. Whether Plaintiffs have shown that the Court should apply the two-way test, instead of the presumptive one-way test, for the Jacobs '690 patent as an obviousness-type double patenting reference to the Patents-in-Suit?

97. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting over claim 3 of the Jacobs '690 patent under the two-way test?

(iii) Obviousness-Type Double Patenting Over the Brockhaus '279 Patent

98. Whether the Brockhaus '279 patent is available as an obviousness-type double patenting reference to invalidate the '182 patent?

99. Whether Plaintiffs have shown that the Asserted Claims of the '182 patent are entitled to claim the protection of the safe harbor under 35 U.S.C. § 121 against a claim of obviousness-type double patenting over the Brockhaus '279 patent?

100. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting over claim 5 of the Brockhaus '279 patent under the one-way test?

101. Whether Plaintiffs have shown that the Court should apply the two-way test, instead of the presumptive one-way test, for the Brockhaus '279 patent as an obviousness-type double patenting reference to the Patents-in-Suit?

102. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for obviousness-type double patenting over claim 5 of the Brockhaus '279 patent under the two-way test?

b. Defendants' Statement of the Issues of Fact to be Litigated

(i) Obviousness-Type Double Patenting Over the Finck '225, '605, and '631 Patents

103. Whether Plaintiff Immunex received all substantive ownership rights to the Patents-in-Suit through the 2004 Accord and Satisfaction Agreement, resulting in Plaintiff Immunex commonly owning each of the Patents-in-Suit and the Finck '225, '605, and '631 patents?

104. Whether the "TNFR:Fc" recited in claim 1 of each of the Finck '225, '605, and '631 patents should be construed to refer to etanercept, as expressly defined in the patent specification?

105. Whether the Asserted Claims of the Patents-in-Suit would have been anticipated or obvious over claim 1 of each of the Finck '225, '605, and '631 patents, which claims a method of treating a patient having psoriasis by administering etanercept?

106. Whether the patent applicants were at least partly responsible for the delay in prosecution of the Patents-in-Suit, which caused the Finck '225 patent to issue before the Patents-in-Suit and the Finck '605 patent to issue before the '182 patent?

(ii) Obviousness-Type Double Patenting Over the Jacobs '690 Patent

107. Whether Plaintiff Immunex received all substantive ownership rights to the Patents-in-Suit through the 2004 Accord and Satisfaction Agreement, resulting in Plaintiff Immunex commonly owning each of the Patents-in-Suit and the Jacobs '690 patent?

108. Whether the "chimeric antibody comprising a TNF receptor comprising the sequence of amino acids 3-163 of SEQ ID NO: 1 fused to the constant domain of an immunoglobulin molecule" recited in claim 3 of the Jacobs '690 patent should be construed to refer to etanercept, in light the specification and prosecution history of the Jacobs '690 patent as well as statements by Plaintiff Immunex in marketing ENBREL® (etanercept)?

109. Whether the Asserted Claims of the Patents-in-Suit would have been anticipated or obvious over claim 3 of the Jacobs '690 patent, which claims a method of lowering the levels of active TNF-α by administering etanercept?

110. Whether the patent applicants were at least partly responsible for the delay in prosecution of the Patents-in-Suit, which caused the Jacobs '690 patent to issue before the Patents-in-Suit?

111. Whether claim 3 of the Jacobs '690 patent would have been anticipated or obvious over any of Asserted Claims of the Patents-in-Suit?

(iii) Obviousness-Type Double Patenting Over the Brockhaus '279 Patent

112. Whether the patent applicants failed to comply with the PTO's restriction requirement and maintain consonance of the line demarking the claimed subject matter of the '182 patent and the Brockhaus '279 patent?

113. Whether the Asserted Claims of the '182 patent would have been obvious over claim 5 of the Brockhaus '279 patent, which claims a fusion protein comprising a soluble fragment of the p55 TNF receptor (instead of the p75 TNF receptor) and the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin?

114. Whether the patent applicants were at least partly responsible for the delay in prosecution of the Patents-in-Suit, which caused the Brockhaus '279 patent to issue before the '182 patent?

115. Whether claim 1 of the Brockhaus '279 patent would have been obvious over any of Asserted Claims of the '182 patent?

c. Defendants' Statement of the Contested Facts

116. ENBREL® (etanercept) was first sold in the United States in November 1998.

117. Immunex obtained several patents covering etanercept, including U.S. Patent No. 5,395,760 ("the Smith '760 patent"), filed May 10, 1990, and U.S. Patent No. 5,605,690 ("the Jacobs '690 patent"), filed Feb. 8, 1995, which had been listed on the label for ENBREL®

(etanercept) from its launch until their expiration. The Smith '760 patent expired in March 2012 and the Jacobs '690 patent expired in February 2014. Separate from the Patents-in-Suit, Immunex has already enjoyed the full-term patent protection (lasting for more than 20 years of exclusivity) covering etanercept.

118. Immunex had also obtained several patents covering a method of treatment by administering etanercept, including each of the Finck patents. The Finck '225 and Finck '605 patents are presently listed on the label for ENBREL® (etanercept).

119. Each of the Asserted Claims of the Patents-in-Suit is invalid for obviousness-type double patenting over each of claim 1 of the Finck '225 patent, claim 1 of the Finck '605 patent, claim 1 of the Finck '631 patent, and/or claim 3 of the Jacobs '690 patent. Each of the Asserted Claims of the '182 patent is invalid for obviousness-type double patenting over claim 5 of the Brockhaus '279 patent.

(i) Immunex is the Owner of the Patents-in-Suit

120. Immunex is the owner of the Patents-in-Suit.

121. In November 1998, Roche had licensed to Immunex the rights to the Brockhaus '790 and '791 applications (which ultimately issued as the Patents-in-Suit) to make, use, and sell its etanercept product for an agreed-upon royalty.

122. In June 2004, Roche and Immunex entered into an "Accord & Satisfaction Agreement," with the express purpose for Immunex "to acquire all rights licensed pursuant to the Roche-Immunex Agreement and to eliminate the continuing obligations to pay royalties to Roche" and for Roche "to sell such rights in accordance with the terms of this [Accord & Satisfaction]." *See* 2004 Accord & Satisfaction Agreement, DTX-357. The 2004 Accord & Satisfaction Agreement transferred to Immunex all substantive ownership rights to the Patents-in-Suit, including the right to exclude all others from practicing the claimed invention, the right

to sue for infringement, the right to grant sublicenses, the right to prosecute and maintain the patent applications at its sole direction, and the right to retain the entirety of any award of damages from a patent infringement suit. *See* 2004 Accord & Satisfaction Agreement, DTX-357.

123. Following execution of the 2004 Accord & Satisfaction Agreement, Roche retained no ownership rights, let alone substantive rights, to the Patents-in-Suit. Immunex owed no continuing obligation to Roche, including no obligation to pay a royalty or share in any award of patent damages concurrent with the execution of the 2004 Accord & Satisfaction Agreement. Thereafter, Immunex was granted the unilateral power to effectively terminate any rights retained by Roche. For example, Roche's illusory right to sue for infringement, only if Immunex failed to do so, may be obviated by Immunex's sole right to grant sublicenses to any alleged infringer.

124. As Immunex acquired the right to prosecute and maintain the patent applications at its sole direction pursuant to the 2004 Accord & Satisfaction Agreement, at the PTO, power of attorney over prosecution of the Patents-in-Suit was transferred exclusively to Immunex. Prosecution History of the '182 patent, DTX-0003, at AMG-ENBNJ-00002225; Prosecution History of the '522 patent, DTX-0004, at AMG-ENBNJ-00008119. Immunex directed and controlled the prosecution of the applications that led to the Patents-in-Suit. In or around 2005, Immunex materially amended the specification and changed the scope of the pending claims in an attempt to purportedly cover etanercept following transfer of control of the prosecution of the applications to Immunex.

(ii) Obviousness-Type Double Patenting Over the Finck '225, '605, and '631 Patents

125. The Finck '225 patent (DTX-11) is titled "Soluble Tumor Necrosis Factor Receptor Treatment of Medical Disorders," and issued on March 29, 2011. The named inventor listed on the face of the Finck '225 patent is Barbara K. Finck.

126. The Finck '225 patent was assigned to Plaintiff Immunex Corporation upon issuance. Plaintiff Immunex Corporation is the owner of the Finck '225 patent.

127. The Finck '225 patent expires on August 13, 2019.

128. Claim 1 of the Finck '225 patent recites as follows:

> 1. A method for treating a patient having psoriasis comprising administering to the patient a therapeutically effective dose of TNFR:Fc, wherein the patient attains at least fifty percent improvement in PASI score.

129. The Finck '225 patent is listed among the patents on the ENBREL® (etanercept) label.

130. The Finck '605 patent (DTX-12) is titled "Soluble Tumor Necrosis Factor Receptor Treatment of Medical Disorders," and issued on February 21, 2012. The named inventor listed on the face of the Finck '605 patent is Barbara K. Finck.

131. The Finck '605 patent was assigned to Plaintiff Immunex Corporation upon issuance. Plaintiff Immunex Corporation is the owner of the Finck '605 patent.

132. The Finck '605 patent expires on August 13, 2019.

133. Claim 1 of the Finck '605 patent recites as follows:

> 1. A method for treating a patient having ordinary psoriasis comprising administering to the patient a therapeutically effective dose of TNFR:Fc.

134. The Finck '605 patent is listed among the patents on the ENBREL® (etanercept) label.

135. The Finck '631 patent (DTX-13) is titled "Soluble Tumor Necrosis Factor Receptor Treatment of Medical Disorders," and issued on May 13, 2014. The named inventor listed on the face of the Finck '631 patent is Barbara K. Finck.

136. The Finck '631 patent was assigned to Plaintiff Immunex Corporation upon issuance. Plaintiff Immunex Corporation is the owner of the Finck '631 patent.

137. The Finck '631 patent expires on August 13, 2019.

138. Claim 1 of the Finck '631 patent recites as follows:

> 1. A method of treatment comprising administering a dose of TNFR:Fc to a patient having psoriatic arthritis and/or plaque psoriasis, wherein the dose is administered one time or two times per week, and wherein the dose administered is 25-50 mg or 50-100 mg, and wherein the dose is administered by subcutaneous injection.

139. The Finck '631 patent is listed among the patents on the ENBREL® (etanercept) label.

140. Claim 1 of each of the Finck '225, '605, and '631 patents anticipates and/or renders obvious each of the Asserted Claims of the Patents-in-Suit.

141. As properly construed, claim 1 of each of the Finck '225, '605, and '631 patents recites a method of treating a patient having psoriasis by administering etanercept. An inherent property of etanercept is specific binding to human TNF. When etanercept is administered to treat a patient having psoriasis, etanercept specifically binds to human TNF. Plaintiffs have not disputed that, if the Finck '225, '605, and '631 patents were reference patents to the Patents-in-Suit, the Asserted Claims of the Patents-in-Suit would not have been patentably distinct under the standard one-way test.

142. Claim 1 of each of the Finck '225, '605, and '631 patents anticipates each of the Asserted Claims of the '182 patent, which claim etanercept and a pharmaceutical composition

comprising etanercept. A person of ordinary skill in the art would have also found the Asserted Claims of the '182 patent obvious in light of the claims of the Finck '225, '605, and '631 patents reciting etanercept.

143. Claim 1 of each of the Finck '225, '605, and '631 patents renders obvious each of the Asserted Claims of the '522 patent. The only difference between the set of claims is that the '522 patent further recites a method for producing etanercept. A person of ordinary skill in the art would have found the claimed method of culturing a host cell (*e.g.*, a CHO cell) comprising a polynucleotide encoding etanercept and purifying etanercept from the cell mass or the cell culture medium to be obvious in light of the claims of the Finck '225, '605, and '631 patents reciting etanercept.

144. Plaintiffs have not shown any objective evidence supporting a finding that the Asserted Claims of the Patents-in-Suit are nonobvious over claim 1 of each of the Finck '225, '605, and '631 patents.

145. Plaintiffs have not shown that the narrow exception for application of the two-way test applies for evaluating the Finck '225, '605, and '631 patents as obviousness-type double patenting references to the Patents-in-Suit. The applications underlying the Finck '631 and '605 patents were filed after the applications underlying the Patents-in-Suit. The Finck '631 patent issued after both of the Patents-in-Suit. *Compare* Finck '631 patent, DTX-13, *with* '182 patent, DTX-1, *and* '522 patent, DTX-2. The Finck '605 patent issued after the '182 patent. *Compare* Finck '605 patent, DTX-12, *with* '182 patent, DTX-1.

146. The PTO was not solely responsible for the delay in causing the Finck '225 patent to issue prior to the Patents-in-Suit or the Finck '605 patent to issue prior to the '182 patent. The patent applicants' dilatory actions during prosecution of the '182 patent included repeatedly

filing and obtaining extensions of time to respond to the PTO's rejections, requesting to reopen prosecution after the PTO found certain claims allowable, and materially amending the specification and changing the scope of the pending claims in an attempt to purportedly cover etanercept following transfer of control of the prosecution of the application to Immunex. The patent applicants' dilatory actions during prosecution of the '522 patent included requesting and ultimately withdrawing a request to initiate interference proceedings, repeatedly filing and obtaining extensions of time to respond to the PTO's rejections, and materially amending the specification and changing the scope of the pending claims in an attempt to purportedly cover etanercept following transfer of control of the prosecution of the application to Immunex. These actions contributed to the delay in issuance of the Patents-in-Suit and, ultimately, unjustly extended their patent term.

(iii) Obviousness-Type Double Patenting Over the Jacobs '690 Patent

147. The Jacobs '690 patent (DTX-17) is titled "Methods of Lowering Active TNF-α Levels in Mammals Using Tumor Necrosis Factor Receptor," and issued on February 25, 1997. The named inventors listed on the face of the Jacobs '690 patent are Cindy A. Jacobs and Craig A. Smith.

148. The Jacobs '690 patent was assigned to Plaintiff Immunex Corporation upon issuance. Plaintiff Immunex Corporation is the owner of the Jacobs '690 patent.

149. The Jacobs '690 patent expired on February 25, 2014. Immunex has already received the full 17-year patent term protection under the Jacobs '690 patent for etanercept.

150. Claim 3 of the Jacobs '690 patent recites as follows:

> 3. A method for lowering the levels of active TNF-α in a mammal in need thereof which comprises administering to said mammal a TNF-lowering amount of a chimeric antibody comprising a TNF

receptor comprising the sequence of amino acids 3-163 of SEQ ID NO:1 fused to the constant domain of an immunoglobulin molecule.

Figure 1 of the Jacobs '690 patent presents a schematic representation of a molecule of etanercept.

151. Prior to its expiration, the Jacobs '690 patent was listed among the patents on the ENBREL® (etanercept) label. *See, e.g.*, DTX-44 at 29; DTX-76 at 34; DTX-77 at 41; DTX-122 at 2; DTX-237 at 35.

152. Claim 3 of the Jacobs '690 patent anticipates and/or renders obvious each of the Asserted Claims of the Patents-in-Suit.

153. As properly construed, the claimed chimeric antibody of claim 3 of the Jacobs '690 patent recites etanercept. Etanercept is a chimeric antibody comprising a TNF receptor comprising the sequence of amino acids 3-163 of SEQ ID NO:1 (*i.e.*, the extracellular region of the p75 TNF receptor) fused to the constant domain of an immunoglobulin molecule (*i.e.*, fused to the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin) as recited in claim 3 of the Jacobs '690 patent. Jacobs '690 patent, DTX-17, at claim 3. This construction is supported by the specification of the Jacobs '690 patent, which provides in Figure 1 a schematic representation of a molecule of etanercept as the preferred embodiment of the patent. *Id.* at Fig. 1. This construction is further consistent with the prosecution history of the Jacobs '690 patent, where Immunex argued to the PTO that the claimed invention had utility based on the results of a clinical trial of etanercept. Prosecution History of Jacobs '690 patent, DTX-18, at SAN-ETAN_0099137-98.

154. Prior to the expiration of the Jacobs '690 patent, Immunex listed the Jacobs '690 patent on the FDA-approved label for ENBREL® (etanercept). *See, e.g.*, DTX-44 at 29; DTX-76 at 34; DTX-77 at 41; DTX-122 at 2; DTX-237 at 35.

155. Claim 3 of the Jacobs '690 patent anticipates each of the Asserted Claims of the '182 patent, which claim etanercept and a pharmaceutical composition comprising etanercept. A person of ordinary skill in the art would have also found the Asserted Claims of the '182 patent obvious in light of claim 3 of the Jacobs '690 patent reciting etanercept.

156. Claim 3 of the Jacobs '690 patent renders obvious each of the Asserted Claims of the '522 patent. The only difference between the set of claims is that the '522 patent further recites a method for producing etanercept. A person of ordinary skill in the art would have found the claimed method of culturing a host cell (*e.g.*, a CHO cell) comprising a polynucleotide encoding etanercept and purifying etanercept from the cell mass or the cell culture medium to be obvious in light of claim 3 of the Jacobs '690 patent reciting etanercept.

157. Plaintiffs have not shown any objective evidence supporting a finding that the Asserted Claims of the Patents-in-Suit are nonobvious over claim 3 of the Jacobs '690 patent.

158. Plaintiffs have not shown that the narrow exception for application of the two-way test applies for the Jacobs '690 patent as an obviousness-type double patenting reference to the Patents-in-Suit. The application underlying the Jacobs '690 patent was filed on February 8, 1995 before the applications underlying the Patents-in-Suit were filed on May 19, 1995. *See* Jacobs '690 patent, DTX-17, at cover. The Jacobs '690 patent issued before each of the Patents-in-Suit. *Id.* The PTO was not solely responsible for the delay in causing the Jacobs '690 patent to issue prior to either the Patents-in-Suit. The patent applicants were partially responsible for

the delay in issuance of the Patents-in-Suit, which ultimately unjustly extended the term of the Patents-in-Suit.

159. Even if the two-way test were applied, the Asserted Claims of the '182 patent render obvious the properly construed claim 3 of the Jacobs '690 patent. The only difference between the set of claims is that the Jacobs '690 patent recites a method comprising administering etanercept to a mammal. A person of ordinary skill in the art would have found it obvious to administer to a mammal a TNF-lowering amount of etanercept to lower the levels of active TNF-α in light of the claims of the '182 patent reciting etanercept.

160. Even if the two-way test were applied, the Asserted Claims of the '522 patent render obvious the properly construed claim 3 of the Jacobs '690 patent. The only difference between the set of claims is that the Jacobs '690 patent recites a method comprising administering etanercept to a mammal. A person of ordinary skill in the art would have found it obvious to administer to a mammal a TNF-lowering amount of etanercept to lower the levels of active TNF-α in light of the claims of the '522 patent reciting etanercept.

161. Plaintiffs have not shown any objective evidence supporting a finding that claim 3 of the Jacobs '690 patent is nonobvious over the Asserted Claims of the Patents-in-Suit.

162. Plaintiffs assert that claim 3 of the Jacobs '690 patent does not recite etanercept. Plaintiffs contend that claim 3 of the Jacobs '690 patent requires a chimeric antibody that includes the CH1 domains and the light chain of an immunoglobulin protein. Plaintiffs proposed construction is inconsistent with the plain meaning of the claims, the specification, and the prosecution history as well as extrinsic evidence of Immunex's representations regarding the scope of the claims of the Jacobs '690 patent.

163. Even if claim 3 of the Jacobs '690 patent were construed to require a chimeric antibody that includes the CH1 domains and the light chain of an immunoglobulin protein, the claim renders obvious each of the Asserted Claims of the Patents-in-Suit. A person of ordinary skill in the art would have motivated to remove the CH1 domain and light chain (resulting in etanercept) in light of the prior art teaching that their removal promotes the expression and secretion of the recombinant protein.

164. Plaintiffs have not shown any objective evidence supporting a finding that the Asserted Claims of the Patents-in-Suit are nonobvious over claim 3 of the Jacobs '690 patent as construed by Plaintiffs.

(iv) Obviousness-Type Double Patenting Over the Brockhaus '279 Patent

165. The Brockhaus '279 patent (DTX-9) is titled "Human TNF Receptor," and issued on March 11, 1997. The named inventors listed on the face of the Brockhaus '279 patent are Manfred Brockhaus, Reiner Gentz, Zlatko Dembic, Werner Lesslauer, Hansruedi Loetscher, and Ernst-Jurgen Schlaeger.

166. The Brockhaus '279 patent was assigned to Plaintiff Roche upon issuance.

167. The Brockhaus '279 patent expired on March 11, 2014.

168. Claim 5 of the Brockhaus '279 patent and the claims upon which it depends recite as follows:

> 1. A recombinant protein encoded by a polynucleotide which comprises two DNA subsequences, wherein the first subsequence encodes a soluble fragment of the insoluble TNF receptor protein, wherein said insoluble TNF receptor protein has a apparent molecular weight of about 55 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, and the second subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region.

> 2. A protein of claim 1 wherein said human immunoglobulin heavy chain is selected from the group consisting of IgG, IgM, IgA and IgE.
>
> 3. A recombinant protein of claim 2, wherein said human immunoglobulin heavy chain is IgG.
>
> 4. A recombinant protein of claim 3, wherein the IgG is IgG1 or IgG3.
>
> 5. A recombinant protein of claim 4, wherein the IgG is IgG1.

169. The '182 patent and the Brockhaus '279 patent share common inventors.

170. Claim 5 of the Brockhaus '279 patent renders obvious each of the Asserted Claims of the '182 patent.

171. As properly construed, claim 5 of the Brockhaus '279 patent recites a recombinant protein encoded by a polynucleotide comprising the DNA sequence of a soluble fragment of the p55 TNF receptor and the DNA sequence for the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin (*i.e.*, all of the domains of the constant region of a human IgG1 immunoglobulin heavy chain other than the first domain of said constant region). Brockhaus '279 patent, DTX-9, at claim 5.

172. As properly construed, claim 5 of the Brockhaus '279 patent renders obvious each of the Asserted Claims of the '182 patent. The only difference between the set of claims is that the TNF receptor fragment in the '182 patent is the extracellular region of the p75 TNF receptor, instead of a soluble fragment of the p55 TNF receptor. A person of ordinary skill in the art would have been motivated to replace the soluble fragment of the p55 TNF receptor in the claimed recombinant protein with the extracellular region of the p75 TNF receptor.

173. Plaintiffs have not shown any objective evidence supporting a finding that the Asserted Claims of the '182 patent are nonobvious over claim 5 of the Brockhaus '279 patent.

174. Plaintiffs have not shown that the narrow exception for application of the two-way test does not apply for the Brockhaus '279 patent as an obviousness-type double patenting reference to the '182 patent. The application underlying the Brockhaus '279 patent was filed on July 21, 1993, before the application underlying the '182 patent was filed on May 19, 1995. Brockhaus '279 patent, DTX-9, at cover; '182 patent, DTX-1, at cover. The Brockhaus '279 patent issued before the '182 patent. *Id.* The PTO was not solely responsible for the delay in causing the Brockhaus '279 patent to issue prior to the '182 patent. The patent applicants were partially responsible for the delay in issuance of the '182 patent, which ultimately unjustly extended the term of the '182 patent.

175. Even if the two-way test were applied, the Asserted Claims of the '182 patent render obvious claim 5 of the Brockhaus '279 patent. The only difference between the set of claims is that the TNF receptor fragment in claim 5 of the Brockhaus '279 patent is a soluble fragment of the p55 TNF receptor, instead of the extracellular region of the p75 TNF receptor. A person of ordinary skill in the art would have been motivated to replace the extracellular region of the p75 TNF receptor with the extracellular region of the p55 TNF receptor (which is a soluble fragment of the p55 TNF receptor).

176. Plaintiffs have not shown any objective evidence supporting a finding that claim 5 of the Brockhaus '279 patent is nonobvious over the Asserted Claims of the '182 patent.

177. Section 121's safe harbor does not apply to exclude the Brockhaus '279 patent as an obviousness-type double patenting reference to the '182 patent.

178. During prosecution of the Brockhaus '279 patent (as the Brockhaus '640 application), the examiner issued a restriction requirement dividing the pending claims into three groups: Group I (the protein and antibody), Group II (the DNA, vector, and host), and Group III

(method of isolating insoluble homogenous proteins). Prosecution History of Brockhaus '279 patent, DTX-6, at AMG-ENBNJ-00354294-98. The examiner further required an election of species within the claims of each of Groups I and II: subgroup A (55 kD TNF receptor) and subgroup B (75 kD TNF receptor). (*Id.*) The patent applicants elected to continue prosecution of the claims in Group IA (the protein and antibody of the p55 TNF receptor). *Id.* at AMG-ENBNJ-00354301. The issued claims of the Brockhaus '279 patent are directed to Group 1A. Brockhaus '279 patent, DTX-9, at claim 5.

179. The patent applicants filed the application underlying the '182 patent (the Brockhaus '790 application) as a divisional application to continue prosecution of the claims in Group IA (the protein and antibody of the p55 TNF receptor), which is the same group of claims as elected in the Brockhaus '279 patent. Prosecution History of the '182 patent, DTX-3, at AMG-ENBNJ-00001359. The patent applicants continued to present claims directed to the fusion protein of the p55 TNF receptor during prosecution of the '182 patent.

180. PTO procedures specifically state that the safe harbor protection does not apply when the claims of the second application are drawn to the same invention as the first invention or parent. (Manual of Patent Examining Procedure, DTX-284, at 30-31.) During prosecution of the '182 patent, the PTO did not afford the application the safe-harbor protections of Section 121. (Prosecution History of the '182 patent, DTX-3, at AMG-ENBNJ-00001638-40; *id.* at AMG-ENBNJ-00004505-11.)

2. Plaintiffs' Statement

181. The judicially created doctrine of obviousness-type double patenting is grounded in 35 U.S.C. § 101—which provides that inventors are entitled to "a patent" for their inventions (subject to the requirements of the Patent Act). *Abbvie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Trust*, 764 F.3d 1366, 1373-74 (Fed. Cir. 2014). This section of the Patent Act

prohibits an inventor from obtaining "more than one patent on the same invention." *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 619 F.3d 1329, 1341 (Fed. Cir. 2010). The doctrine of obviousness type double patenting extended this prohibition to preclude an applicant from obtaining two patents that covered "slight variants" of the same invention thus "prevent[ing] issuance of a patent on claims that are nearly identical to claims" in another patent. *Id.*

182. Obviousness-type double patenting is applicable only where there is at least one inventor in common between a challenged patent and a reference patent, or where the "common ownership" requirement is met.[15] *In re Hubbell*, 709 F.3d 1140, 1148 (Fed. Cir. 2013).

183. No court has ever applied the "all substantial rights test"—which Defendants attempt to borrow from the law of prudential standing—to determine "common ownership" for purposes of obviousness-type double patenting.

184. Both of the cases Sandoz relies on for the "all substantial rights test," *supra*, ¶ 97, apply the test to prudential standing and do not discuss how "common ownership" is defined for the purposes of obviousness-type double patenting. *See Speedplay, Inc. v. Bebop, Inc.*, 211 F.3d 1245, 1249-50 (Fed. Cir. 2000); *see also Diamond Coating Techs., LLC v. Hyundai Motor Am.*, 823 F.3d 615, 618-19 (Fed. Cir. 2016).

185. No court has ever treated a license agreement as transferring ownership and creating "common ownership" for purposes of obviousness-type double patenting.

186. No court has ever indicated that anything less than 100% common ownership will suffice for purposes of the "common ownership" requirement.

[15] As explained below, the parties dispute the contours of the common ownership requirement, including the applicable test for determining common ownership and the relevant time period in which common ownership must exist.

187. Consistent with § 101, obviousness-type patenting attaches where patents share a common inventor or common ownership at the time of invention, prohibiting inventors or those who own an invention from pursuing multiple patents on the same or patentably indistinct inventions. Double patenting thus does not apply when patents are licensed or transferred long after the time of invention, and no court has invoked double patenting to invalidate a patent based on a license agreement entered into many years after an invention was made.

188. In the limited circumstances where obviousness-type double patenting may apply, the analysis involves two steps:

- First, the court construes the claims in the earlier patent and the claims in the later patent and determines the differences.
- Second, the court determines, on a claim-by-claim basis, whether those differences render the claims patentably distinct.

189. A later claim that is not patentably distinct from, *i.e.*, is obvious over or anticipated by, an earlier claim is invalid for obviousness-type double patenting. *Abbvie*, 764 F.3d at 1374. The obviousness analysis in the context of obviousness-type double patenting includes consideration of objective indicia of non-obviousness. *Eli Lilly*, 689 F.3d at 1381.

190. In assessing whether the claims of a challenged patent and a reference patent are patentably distinct, the subject matter of each of the claims must be considered as a whole. *See Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1278 (Fed. Cir. 1992) ("Claims must be read as a whole in analyzing a claim of double patenting.").

191. 35 U.S.C. § 121 provides a safe harbor that prevents an earlier issued patent from being used as a reference to challenge the validity of a later issued patent if a restriction requirement was made by the Patent Office during prosecution of the application that resulted in

the earlier issued patent and the later issued patent issued from a divisional application of the application that resulted in the earlier issued patent.

192. If a restriction requirement is made by the Patent Office during prosecution that requires the applicant to elect a species within a genus, an application and patent that claims that species falls under the safe harbor provisions of 35 U.S.C. § 121. *See St. Jude Med., Inc. v. Access Closure, Inc.*, 729 F.3d 1369, 1378-79 (Fed. Cir. 2013); *see also* Manual of Patenting Examining Procedure (MPEP) § 806.04(d), 8th Edition, Rev. 8 (July 2010).

193. Sandoz alleges that the Asserted Claims are invalid for obviousness-type double patenting.[16]

194. Pursuant to the Amended Stipulation (D.I. 510 ¶ 3.a), Sandoz has identified three double-patenting reference families: U.S. Patent Nos. 7,915,225 ("Finck '225 patent"), 8,119,605 ("Finck '605 patent"), and 8,722,631 ("Finck '631 patent"); U.S. Patent No. 5,605,690 ("Jacobs '690 patent"); and U.S. Patent No. 5,610,279 ("Brockhaus '279 patent").[17]

195. Specifically, Sandoz alleges that the Asserted Claims are not patentably distinct from claim 1 of the Finck '225 patent, which recites:

> A method for treating a patient having psoriasis comprising administering to the patient a therapeutically effective dose of TNFR:Fc, wherein the patient attains at least fifty percent improvement in PASI score.

196. Sandoz also alleges that the Asserted Claims are not patentably distinct from claim 1 of the Finck '605 patent, which recites:

[16] Joint Pretrial Report. D.I. 486.

[17] *See* June 5, 2018 Sandoz's Disclosure of Obviousness Combinations and Double Patenting Reference Families (attached as **Joint Exhibit 2**).

> A method for treating a patient having ordinary psoriasis comprising administering to the patient a therapeutically effective dose of TNFR:Fc.

197. Sandoz also alleges that the Asserted Claims are not patentably distinct from claim 1 of the Finck '631 patent, which recites:

> A method of treatment comprising administering a dose of TNFR:Fc to a patient having psoriatic arthritis and/or plaque psoriasis, wherein the dose is administered one time or two times per week, and wherein the dose administered is 25-50 mg or 50-100 mg, and wherein the dose is administered by subcutaneous injection.

198. Sandoz also alleges that the Asserted Claims are not patentably distinct from claim 3 of the Jacobs '690 patent, which recites:

> A method for lowering the levels of active TNF-α in a mammal in need thereof which comprises administering to said mammal a TNF-lowering amount of a chimeric antibody comprising a TNF receptor comprising the sequence of amino acids 3-163 of SEQ ID NO:1 fused to the constant domain of an immunoglobulin molecule.

199. Sandoz also alleges that the Asserted Claims are not patentably distinct from claim 5 of the Brockhaus '279 patent, which recites:

> A recombinant protein encoded by a polynucleotide which comprises two DNA subsequences, wherein the first subsequence encodes a soluble fragment of the insoluble TNF receptor protein, wherein said insoluble TNF receptor protein has a apparent molecular weight of about 55 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, and the second subsequence encodes all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region [wherein the immunoglobulin heavy chain is IgG1].

200. Plaintiffs dispute Sandoz's allegations of obviousness-type double patenting.

201. As with obviousness under 35 U.S.C. § 103, obviousness-type double patenting is a question of law premised on underlying factual inquiries, including findings regarding objective indicia, considered in a Section 103 obviousness analysis. *Eli Lilly*, 689 F.3d at 1376.

202. Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut the presumption of validity, Defendants bear the burden of proving invalidity by clear and convincing evidence, *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 110-14 (2011), and that "ultimate burden never shifts." *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1329 (Fed. Cir. 2008); *see also Symbol Techs., Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1580 (Fed. Cir. 1991) (explaining that defendant was "required to prove double patenting by clear and convincing evidence, a heavy and unshifting burden"). Defendants' suggestion that Plaintiffs bear the burden of proof or the burden of persuasion with respect to certain double-patenting issues is therefore misplaced. To the extent that fact questions arise—regarding, for example whether all substantial rights were transferred under the Accord & Satisfaction, or who was responsible for delays at the Patent Office during a relevant period—Sandoz bears the burden of proving any necessary facts by clear and convincing evidence.

a. Plaintiffs' Statement of Issues of Law to Be Litigated

203. Whether Defendants have proven, by clear and convincing evidence, that each of the Asserted Claims of the '182 patent is invalid for obviousness-type double patenting based on one or more of the three purported reference families identified by Defendants.

204. Whether Defendants have proven, by clear and convincing evidence, that each of the Asserted Claims of the '522 patent is invalid for obviousness-type double patenting based on one or more of the three purported reference families identified by Defendants.

205. Whether Defendants have proven, by clear and convincing evidence, that the doctrine of obviousness-type double patenting can apply where the challenged patent and reference patent share no common inventors and the owner of the challenged patent at the time of its invention and the owner of the reference patent at the time of its invention are not the same.

206. In the absence of any common inventors, what must Defendants prove by clear and convincing evidence in order to establish the "common ownership" requirement under the obviousness-type double patenting doctrine, including but not limited to:

- Whether Defendants must prove "common ownership" of the challenged and reference patents by the same legal entity, and if not, what relationship between legally distinct entities is sufficient for Defendants to prove "common ownership";
- Whether Defendants must prove "common ownership" of the challenged and reference patent by showing identity (or some other specific relationship) between the entity that owned the challenged patent at the time of its invention and the entity that owned the reference patent at the time of its invention, rather than at a later time; and
- If Defendants have proven, by clear and convincing evidence, that the obviousness type double patenting doctrine allows an entity that did not own a challenged patent at the time of its invention to become a "common owner" after-the-fact—whether such after-the-fact "common ownership" can be established by acquisition of less than all rights in a patent (rather than ownership-in-fact), and if so, what requirements such after-the-fact acquisition must have.

207. Whether Defendants have proven by clear and convincing evidence that the patent-term protection afforded by Congress to patents issuing from pre-GATT patent applications can be vitiated by operation of the judicially-created doctrine of obviousness-type double patenting based on a patent issuing from a post-GATT patent application.[18]

[18] Patents that mature from applications filed before the June 8, 1995 effective date of the Uruguay Round of the General Agreement on Tariffs and Trade and Trade-Related Aspects of Intellectual Property are commonly referred

The Finck Patents

208. Whether Defendants have proven, by clear and convincing evidence, that the Finck Patents, which issued from post-GATT applications, are available as potential references in an obviousness-type double patenting challenge against the Asserted Claims (given that Patents-in-Suit issued from pre-GATT applications).

209. Whether Defendants have proven, by clear and convincing evidence, that the Finck Patents satisfy the common ownership requirement necessary to allow them to be available as potential references in an obviousness-type double patenting challenge against the Patents-in-Suit, including but not limited to:

- Whether the Finck Patents and the Patents-in-Suit are entirely owned by the same entity;
- Whether Defendants have proven by clear and convincing evidence that the entity that owned the Patents-in Suit at the time of their invention also owned the Finck Patents' at the time of their invention; and
- If Defendants have proven, by clear and convincing evidence, (i) that the obviousness type double patenting doctrine allows an entity that did not own a challenged patent at the time of its invention to become a "common owner" after-the-fact, and (ii) that such after-the-fact "common ownership" can be established by acquisition of less than all rights in a patent—whether Defendants have proven by clear and convincing evidence that the 2004 Accord & Satisfaction conveyed

to as "pre-GATT" patents. *E.g.*, *Gilead Sciences Inc. v. Natco Pharma Ltd.*, 753 F.3d 1208, 1211 (Fed. Cir. 2014). Applications filed after June 8, 1995 are commonly referred to as "post-GATT" patents. *Id.* The Patents-in-Suit are pre-GATT patents because they were filed before June 8, 1995.

to Immunex sufficient rights to establish Immunex as the owner, rather than the exclusive licensee, of the Patents-in-Suit.

210. If Sandoz has proven, by clear and convincing evidence, that the Finck Patents are available as potential references in an obviousness-type double patenting challenge against the Patents-in-Suit—whether Defendants have proven, by clear and convincing evidence, that the "two-way test" for determining patentable distinctness does not apply, notwithstanding the fact that there was no applicant-caused delay in the prosecution of the Patents-in-Suit during the period that the applications that resulted in the Finck Patents and the applications that resulted in the Patents-in-Suit were co-pending, or even during the period that they were allegedly "co-owned."

211. If Sandoz has proven, by clear and convincing evidence, that the Finck Patents are available as potential references in an obviousness-type double patenting challenge against the Patents-in-Suit,:

- The meaning of (i) claim 1 of the Finck '225 patent, (ii) claim 1 of the Finck '605 patent, and (iii) claim 1 of the Finck '631 patent;
- Whether Defendants have proven by clear and convincing evidence that the Asserted Claims are not patentably distinct from (i) claim 1 of the Finck '225 patent, (ii) claim 1 of the Finck '605 patent, and (iii) claim 1 of the Finck '631 patent;
- Whether the law allows the use of a single limitation from claim 1 of the Finck '225 patent, claim 1 of the Finck '605 patent, and claim 1 of the Finck '631 patent, rather than the invention claimed as a whole in these claims, to invalidate the Asserted Claims; and

- If Defendants have failed to prove, by clear and convincing evidence, that the "two-way test" for determining patentable distinctness does not apply, whether Defendants have proven by clear and convincing evidence that the Asserted Claims would render obvious the methods of treatment (i.e., psoriasis and/or psoriatic arthritis) claimed in (i) claim 1 of the Finck '225 patent, (ii) claim 1 of the Finck '605 patent, and (iii) claim 1 of the Finck '631 patent.

The Jacobs '690 Patent

212. Whether Defendants have proven, by clear and convincing evidence, that the Jacobs '690 patent satisfies the common ownership requirement necessary to allow it to be available as a potential reference in an obviousness-type double patenting challenge against the Patents-in-Suit, including but not limited to:

- Whether Defendants have proven by clear and convincing evidence that the Jacobs '690 patent and the Patents-in-Suit are entirely owned by the same entity;
- Whether Defendants have proven by clear and convincing evidence that the entity that owned the Patents-in-Suit at the time of their invention also owned the Jacobs '690 patent at the time of its invention; and
- If Defendants have proven, by clear and convincing evidence, (i) the obviousness-type double-patenting doctrine allows an entity that did not own a challenged patent at the time of its invention to become a "common owner" after-the-fact, and (ii) that such after-the-fact "common ownership" can be established by less than all rights in a patent—whether Defendants have proven by clear and convincing evidence that the 2004 Accord & Satisfaction conveyed to Immunex

sufficient rights to establish Immunex as the owner, rather than the exclusive licensee, of the Patents-in-Suit.

213. If Sandoz has proven, by clear and convincing evidence, that the Jacobs '690 patent is available as a potential reference in an obviousness-type double patenting challenge against the Patents-in-Suit:

- The meaning of claim 3 of the Jacobs '690 patent, including the meaning of the term "chimeric antibody comprising the sequence of the amino acids 3-163 of SEQ ID NO:1 fused to the constant domain of an immunoglobulin";
- Whether Defendants have proven by clear and convincing evidence that the Asserted Claims are not patentably distinct from claim 3 of the Jacobs '690 patent; and
- Whether the law allows the use of a single limitation from claim 3 of the Jacobs '690 patent, rather than the invention claimed as a whole in this claim, to invalidate the Asserted Claims.

The Brockhaus '279 Patent

214. Whether Defendants have proven, by clear and convincing evidence, that the safe harbor of 35 U.S.C. § 121 does not protect the '182 patent against a double-patenting challenge based on the Brockhaus '279 patent, given that the claims of the '182 patent arose after a restriction requirement made by the USPTO requiring the applicant to elect between subject matter encompassing the p55 TNF receptor protein or the p75 TNF receptor protein and, as issued, are in consonance with the subject matter of the restriction requirement.

215. Whether Defendants have proven, by clear and convincing evidence, that the safe harbor of 35 U.S.C. § 121 does not protect the '522 patent against a double-patenting challenge

based on the Brockhaus '279 patent, given that the claims of the '522 patent arose after a restriction requirement made by the USPTO requiring the applicant to elect between subject matter encompassing proteins and antibodies, on the one hand, and DNA, vector, and host, on the other hand, as well as between subject matter encompassing the p55 TNF receptor protein or the p75 TNF receptor protein, and are in consonance with the subject matter of the restriction requirement.

216. If Defendants have proven, by clear and convincing evidence, that the safe harbor of 35 U.S.C. § 121 does not apply to either or both of the Patents-in Suit:

- The meaning of claim 5 of the Brockhaus '279 patent;
- Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the '182 patent and/or the '522 patent (as applicable) are not patentably distinct from claim 5 of the Brockhaus '279 patent; and
- Whether the law allows the use of select limitations from claim 5 of the Brockhaus '279 patent, rather than the invention claimed as a whole in this claim, to invalidate the applicable Asserted Claims.

b. Plaintiffs' Statement of Issues of Fact to Be Litigated[19]

217. If Defendants have proven, by clear and convincing evidence, (i) that the obviousness type double patenting doctrine allows an entity that did not own a challenged patent

[19] Defendants wrongly claim that Plaintiffs' statements regarding the "contested facts" are improper. *See, supra*, § VII.A.2, footnote 19. While the parties agreed to follow a model pretrial order, the "contested facts" section of that model sets out each side's "*additional* proposed stipulation of facts." Hence, this section includes general scientific facts, and other basic issues, for which the parties were apparently unable to sufficiently agree to for inclusion in the "stipulation of facts" section of the model order. The "contested facts" section was not intended to set out (even at a high level) the issues of fact to be litigated in the case, as borne out by the fact the accused infringer in that case identified only three "*additional* proposed stipulation of facts," in a case involving issues of infringement, anticipation, obviousness, obviousness-type double patenting, lack of written description and enablement, inequitable conduct, etc.

at the time of its invention to become a "common owner" after-the-fact, and (ii) that such after-the-fact "common ownership" can be established by acquisition of less than all rights in a patent—whether Defendants have proven by clear and convincing evidence that the parties to the 2004 Accord & Satisfaction intended to and did convey to Immunex sufficient rights to establish Immunex as the owner, rather than the exclusive licensee, of the Patents-in-Suit.[20]

218. If Sandoz has proven, by clear and convincing evidence, that the Finck Patents are available as potential references in an obviousness-type double patenting challenge against the Patents-in-Suit:

- The differences between (i) claim 1 of the Finck '225 patent and the Asserted Claims, (ii) claim 1 of the Finck '605 patent and the Asserted Claims, and (iii) claim 1 of the Finck '631 patent and the Asserted Claims;
- The level of ordinary skill in the art;
- Whether Defendants have proven, by clear and convincing evidence, that there was a motivation, with a reasonable expectation of success, to treat psoriasis and/or psoriatic arthritis with "TNFR:Fc" at the time of the invention; and
- Whether, once established by Plaintiffs, Defendants have rebutted, by clear and convincing evidence, the objective indicia of non-obviousness.

219. If Sandoz has proven, by clear and convincing evidence, that the Finck Patents are available as potential references in an obviousness-type double patenting challenge against the Patents-in-Suit—whether Sandoz has proven, by clear and convincing evidence, that there was any delay caused by applicants during any period in which the applications that resulted in the

[20] Immunex is the assignee of the Finck Patents and the Jacobs '690 patent, having obtained assignments from the inventors of these patents. Roche is the assignee of Patents-in-Suit, having obtained assignments from the inventors of the Patents-in-Suit.

Finck Patents and the applications that resulted in the Patents-in-Suit were co-pending, or even the period in which they were allegedly co-owned.

220. If Sandoz has proven, by clear and convincing evidence, that the Jacobs '690 patent is available as a potential reference in an obviousness-type double patenting challenge against the Patents-in-Suit:

- The differences between claim 3 of the Jacobs '690 patent and the Asserted Claims;[21]
- The level of ordinary skill in the art;
- Whether Defendants have proven, by clear and convincing evidence, that there was a motivation, with a reasonable expectation of success, to modify the "chimeric antibody" of claim 3 of the Jacobs '690 patent (which comprises a fragment of the extracellular region of the p75 TNF receptor "fused to the constant domain of an immunoglobulin molecule") to arrive at a fusion protein that meets each and every limitation of the Asserted Claims at the time of the invention (which consists of the entire extracellular region of the p75 TNF receptor fused to "all of the domains of the constant region…other than the first domain of said constant region"); and
- Whether, once established by Plaintiffs, Defendants have rebutted, by clear and convincing evidence, the objective indicia of non-obviousness.

[21] Defendants now claim that the "only difference between" claim 3 of the Jacobs '690 patent and the Asserted Claims of the '522 patent is that the Asserted Claims "further recites a method for producing etanercept." *See, supra*, ¶ 168. Plaintiffs dispute that this is the only difference between claim 3 of the Jacobs '690 patent and the subject matter of the Asserted Claims.

221. If Sandoz has proven, by clear and convincing evidence, that the Brockhaus '279 patent is available as a potential reference in an obviousness-type double patenting challenge against the Patents-in-Suit—whether Sandoz has proven, by clear and convincing evidence:

- The differences between claim 5 of the Brockhaus '279 patent and the applicable Asserted Claims;
- The level of ordinary skill in the art;
- Whether Defendants have proven, by clear and convincing evidence, that there was a motivation, with a reasonable expectation of success, to modify the "recombinant protein" of claim 5 of the '279 patent (which comprises a genus of fusion proteins that include any "soluble fragment of the insoluble" p55 TNF receptor) to arrive at a fusion protein that meets each and every limitation of the Asserted Claims at the time of the invention (which consists of the entire extracellular region of the p75 TNF receptor fused to "all of the domains of the constant region...other than the first domain of said constant region"); and
- Whether, once established by Plaintiffs, Defendants have rebutted, by clear and convincing evidence, the objective indicia of non-obviousness.

c. Response to Defendant's Statement of Contested Facts

222. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section above. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

C. Obviousness (35 U.S.C. § 103)

1. Defendants' Statement

223. "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a).

224. "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unresolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy." *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

225. The Supreme Court has adopted an "expansive and flexible approach" to question of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007). For example, "[w]hen a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." *Id.* at 417.

226. In the context of new chemical compounds, "the accused infringer must identify some reason that would have led a chemist to modify a known compound." *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 973 (Fed. Cir. 2014). "The motivation to modify that lead compound can come from any number of sources and need not necessarily be explicit in the art. '[I]t is sufficient to show that the claimed and prior art compounds possess a sufficiently close relationship ... to create an expectation, in light of the totality of the prior art, that the new compound will have similar properties to the old.'" *Id.*

227. Evidence of simultaneous invention by those working in the field is relevant evidence to show that the motivation to combine the elements of the prior art according to the claimed invention is not the result of any hindsight bias. *International Glass Co. v. U.S.*, 408 F.2d 395, 405 (Ct. Cl. 1969) ("The problem of hindsight [in an obviousness analysis] is greatly minimized in this case where there is evidence of the level of ordinary skill in the art and how those skilled in the art approached and solved problems" addressed by the claimed invention.). "The fact of near-simultaneous invention, though not determinative of statutory obviousness, is strong evidence of what constitutes the level of ordinary skill in the art." *Id.* Thus, "[i]ndependently made, simultaneous inventions, made 'within a comparatively short space of time,' are persuasive evidence that the claimed apparatus 'was the product only of ordinary mechanical or engineering skill.'" *Geo. M. Martin Co. v. Alliance Machine Sys. Intern. LLC*, 618 F.3d 1294, 1305-06 (Fed. Cir. 2010) (finding that a machine "occurring only a year later than the earliest possible reduction-to-practice date of the claimed invention, qualified as a simultaneous invention" supporting obviousness).

228. Copying in the context of regulatory approval of a drug product is not probative evidence of nonobviousness. The BPCIA established an abbreviated pathway for the approval of

biological drugs that meet the requirements for biosimilarity to a previously approved reference biological drug. 42 U.S.C. § 262(k). Biosimilarity requires evidence that: "(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and (B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." 42 U.S.C. § 262(i)(2). FDA Guidance confirms this. In the similar context of abbreviated new drug applications, copying has been found to have no probative value to the question of nonobviousness. *Bayer Healthcare Pharm., Inc. v. Watson Pharm., Inc.*, 713 F.3d 1369, 1377 (Fed. Cir. 2013) (explaining that copying is "not probative of nonobviousness" in pharmaceutical cases because "a showing of bioequivalence is required for FDA approval"); *see also Purdue Pharma Prod. L.P. v. Par Pharm., Inc.*, 377 F. App'x 978, 983 (Fed. Cir. 2010) (same); *Hoffmann-La Roche Inc. v. Apotex Inc.*, No. 07 4417, 2012 WL 1637736, at *20 (D.N.J. May 7, 2012) (same).

a. Defendants' Statement of the Issues of Law to be Litigated

229. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid as obvious to a person of ordinary skill in the art as of August 1990 pursuant to 35 U.S.C. § 103?

b. Defendants' Statement of the Issues of Fact to be Litigated

230. What are the qualifications of a person of ordinary skill in the art?

231. Whether the scope and content of the prior art as of August 1990 describes each of the elements of the Asserted Claims of the Patents-in-Suit?

232. What are the differences between the claimed invention and the prior art?

233. Whether a person of ordinary skill in the art as of August 1990 would have been motivated to develop a fusion protein consisting of the extracellular region of the p75 TNF

receptor and the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin, with a reasonable expectation of success, in light of the prior art?

234. Whether a person of ordinary skill in the art as of August 1990 would have been motivated to culture a host cell comprising the polynucleotide encoding the claimed fusion protein and to purify the fusion protein from the cell culture medium, with a reasonable expectation of success?

235. Whether the objective indicia support the obviousness of the Asserted Claims of the Patents-in-Suit?

c. Defendants' Statement of the Contested Facts

236. Each of the Asserted Claims of the Patents-in-Suit would have been obvious to a person of ordinary skill in the art as of August 31, 1990.

237. Real-world evidence shows that several research groups—namely, Immunex and Behringwerke, UT Southwestern, and Genentech—before and shortly after August 1990 had the idea and independently developed TNF receptor-IgG fusion proteins. In particular, independent of any involvement of Plaintiff Roche, scientists at Immunex and Behringwerke had developed a p75 TNF receptor-IgG1 fusion protein prior to August 1990 and had developed the specific etanercept protein by November 1990. Scientists at Roche did not conceive of or make etanercept. Immunex relies on its own research to argue that the patents filed by Roche scientists are nonobvious.

(i) Level of Ordinary Skill in the Art

238. A person of ordinary skill in the art with respect to the claimed subject matter of the Patents-in-Suit would include a person who possess a M.D. or Ph.D. in biology, molecular biology, biochemistry, chemistry, or a similar field with 1-2 years of experience in the field of

immunology or molecular immunology, including experience with cloning and expression of DNA, protein biochemistry, cell culture, protein purification, and immunological assays.

(ii) Scope and Content of the Prior Art As of August 1990[22]

239. The Asserted Claims of the Patents-in-Suit would have been obvious to a person of ordinary skill in the art in August 1990 in light of the prior art relating to (1) the TNF receptors and (2) fusion proteins containing a portion of a receptor fused to a portion of an immunoglobulin including human IgG1 at different junctions, including the "hinge" region. It is undisputed that by August 1990 the receptor-IgG1 fusion proteins were shown to enhance the properties of the soluble receptors. Prior art examples of receptor-IgG1 fusion proteins include fusion proteins that fuse the soluble ligand-binding portion of CD4 to the hinge-CH2-CH3 portion of a human IgG1 (*e.g.*, the Seed '262 publication, and Byrn 1990) and fusion proteins that fuse the soluble ligand-binding portion of a homing receptor to the hinge-CH2-CH3 portion of a human IgG1 (*e.g.*, Capon '964 patent and Watson 1990).

240. Tumor necrosis factor-α and –β, collectively referred to as "TNF," are small proteins that are involved in cell signaling, which is a means by which cells perceive and respond to their extracellular environment. This was well established as of August 1990 and is not disputed. The messenger of the signals, such as TNF, is referred to as a "ligand." When a ligand binds to its receptor on the outside of a cell, the receptor transmits the signal to the inside of the cell, leading to various physiological effects.

241. By August 1990, scientists had identified two cell-surface receptors that specifically bind TNF: the p55 TNF receptor and the p75 TNF receptor. *See* Brockhaus 1990,

[22] On July 13, 2018, Defendants identified background references describing aspects of the state of the prior art in August 1990 for purposes of demonstrating Defendants' case of *prima facie* obviousness. *See* Letter from Maureen Rurka to Vernon M. Winters (July 13, 2018).

DTX-36, at 3127. The DNA and amino acid sequences for both receptors were reported in the prior art by August 1990. *See, e.g.*, Loetscher 1990, DTX-47, at Figure 2A; Schall 1990, DTX-34, at Figure 1; Smith '760 patent, DTX-45, at Figures 2A-2B; Smith 1990, DTX-24, at Figure 3. Plaintiffs' experts do not dispute these facts.

242. By August 1990, TNF was known to cause a biological effect on cells by binding to the TNF receptors that are expressed on the cell surface of TNF-responsive cells. The overproduction of TNF was shown to be associated with significant harmful effects on the body, including causing diseases, such as rheumatoid arthritis where the body's immune system begins to attack healthy tissue. *See, e.g.*, Brennan 1989, DTX-75, at 244; Hinshaw 1990, DTX-79, at 279; Jacob 1989, DTX-127, at 254. A known strategy for mitigating diseases that are caused by the overstimulation of a cell signaling pathway is to inhibit the binding of the ligand to its cell-surface receptor. For example, this binding may be inhibited by administering the soluble form of the receptor (*i.e.*, the extracellular region of the receptor that is no longer attached to the cell), which acts as a "decoy" receptor that binds to the ligand, thereby leaving less ligand available to bind to the cell-surface receptor. *See, e.g.*, Smith '760 patent, DTX-45, at col. 2, l. 67 – col. 3, l. 6; Capon '964 patent, DTX-43, at col. 4, ll. 16-20. None of these facts are in dispute.

243. By August 1990, scientists had isolated in human blood and urine naturally-occurring TNF-binding proteins that were believed to play an important physiological role in inhibiting the binding of TNF to its cell-surface receptor. *See, e.g.*, Seckinger 1989, DTX-21, at 11966; Seckinger 1990b, DTX-29, at 5188; Engelmann 1989, DTX-51, at 11974; Engelmann 1990, DTX-49, at 1531. These TNF-binding proteins had been identified as the extracellular regions of the TNF receptors, which had been enzymatically cleaved at the cell surface to form a

soluble TNF receptor. *See id.*; *see also* Loetscher 1990, DTX-47, at 354; Schall 1990, DTX-34, at 361. None of these facts are in dispute.

244. By August 1990, the prior art taught administering a soluble form of the TNF receptor or other TNF-binding protein derived from the soluble form of the TNF receptor as a potential therapeutic agent to target TNF and inhibit its binding to its cell-surface receptors. *See, e.g.*, Wallach '378 publication, DTX-38; Hohmann 1989, DTX-52; Loetscher 1990, DTX-47; Schall, DTX-34; Smith '760 patent, DTX-45; Smith 1990, DTX-24. These soluble forms comprising the extracellular region of the TNF receptor were shown known to bind TNF with high affinity. This is not disputed.

245. By August 1990, the prior art taught the construction of fusion proteins that fused the soluble, TNF-binding portion of a p75 TNF receptor to a portion of a human IgG1. For example, the Smith '760 patent taught that the construction of both a soluble p75 TNF receptor and a chimeric antibody comprised of the soluble p75 TNF receptor fused to the constant domains of an IgG1 immunoglobulin, which are both useful in diagnostic assays to study TNF and in therapy to bind or scavenge for TNF. *See* Smith '760 patent, DTX-45, at col. 2, l. 67 – col. 3, l. 6, col. 9, ll. 17-29, col. 10, ll. 53-61. This is not disputed.

246. By August 1990, the prior art taught that the properties of the soluble receptor (*e.g.*, CD4, lymphocyte homing receptor, and others) may be enhanced by developing receptor-IgG1 fusion proteins, including by joining the soluble receptor to the hinge-CH2-CH3 portion of an IgG1. *See, e.g.*, Seed '262 publication, DTX-33; Capon 1989, DTX-23; Traunecker 1989, DTX-25; Capon '964 patent, DTX-43; Byrn 1990, DTX-22; Watson 1990, DTX-30. Fusing soluble receptors to the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin were shown to provide several advantages, including (i) extending the half-life of the soluble receptor *in vivo*,

(ii) providing for a bivalent structure that can enhance binding of the receptor to its ligand, and (iii) allowing for purification of the receptor using standard affinity chromatography techniques. The DNA and amino acid sequences of the human IgG1 immunoglobulin, including the sequences for the hinge-CH2-CH3 portion, were known by August 1990. This is not disputed.

247. By August 1990, the recombinant DNA technology had developed routine techniques for cutting and fusing DNA molecules together to form a fusion DNA sequence. Routine techniques allowed for the production of fusion proteins using suitable vectors to introduce the DNA sequence into host cells and to culture the host cells to express the fusion protein. This is not disputed.

248. By August 1990, the prior art taught the receptor-IgG1 fusion proteins have broad usefulness as inhibitors to block the binding of a ligand to its receptor in conditions aggravated by the ligand-receptor binding. *See, e.g.,* Traunecker 1989, DTX-25, at 70; Capon '964 patent, DTX-43, at col. 4, ll. 16-20, 38-41; Watson 1990, DTX-30, at 2221, 2228. The prior art teaches the use of these receptor-IgG1 fusion proteins as therapeutic agents in immune and inflammatory diseases, including rheumatoid arthritis. *See, e.g.*, Capon' 964 patent, DTX-43, at col. 30, ll. 42-48; Watson 1990, DTX-30, at 2228.

(iii) Motivation to Combine and Reasonable Expectation of Success As of August 1990

249. The prior art collectively teach and would have motivated a person of ordinary skill in the art to develop a fusion protein capable of specifically binding TNF consisting of the extracellular region of the p75 TNF receptor fused to the hinge-CH2-CH3 portion of an IgG1 immunoglobulin. The amino acid and DNA sequences of both the p75 TNF receptor and the IgG immunoglobulin were known and published in the prior art by August 1990.

250. A person of ordinary skill in the art in August 1990 would have been motivated to develop a TNF-binding protein, including as a tool to study TNF and its mechanism of action and as a potential therapeutic agent to inhibit the role of TNF in mediating certain inflammatory and immune diseases.

251. A person of ordinary skill in the art in August 1990 would have been motivated to select the extracellular region of the p75 TNF receptor, which was shown to specifically bind TNF, as a starting point in developing a TNF-binding protein. A person of ordinary skill in the art in August 1990 would have been motivated to fuse the extracellular region of the p75 TNF receptor to an IgG1 immunoglobulin, including to extend the half-life of the receptor, enhance the binding of the receptor to TNF, and permit use of standard techniques to purify the receptor. A person of ordinary skill in the art in August 1990 would have been motivated to fuse the extracellular region of the p75 TNF receptor at the hinge of an IgG1 immunoglobulin (thereby, leaving the hinge-CH2-CH3 domain), because the prior art taught that removal of the CH1 domain and the light chain of an IgG1 immunoglobulin facilitated the expression and secretion of the fusion protein.

252. A person of ordinary skill in the art in August 1990 also would have been motivated to select the p75 TNF receptor-IgG chimeric antibody of Smith '760 patent, which was expected to provide for extended half-life, enhanced binding to TNF, and use of standard purification techniques, as a starting point in developing a TNF-binding protein. A person of ordinary skill in the art in August 1990 would have been motivated to remove the CH1 domain and the light chain of the chimeric antibody to facilitate the expression and secretion of the protein.

253. A person of ordinary skill in the art in August 1990 would have been motivated to culture a host cell (*e.g.*, a CHO cell) comprising a polynucleotide that encodes a fusion protein consisting of the extracellular region of the p75 TNF receptor fused to the hinge-CH2-CH3 portion of a human IgG1, and would have been motivated to purify the expressed fusion protein from the cell mass or culture medium.

254. A person of ordinary skill in the art in August 1990 would reasonably expect that a fusion protein consisting of the extracellular region of the p75 TNF receptor fused to the hinge-CH2-CH3 portion of an IgG1 immunoglobulin would specifically bind to human TNF.

255. A person of ordinary skill in the art in August 1990 would have been able to successfully express and purify a fusion protein consisting of the extracellular region of the p75 TNF receptor fused to the hinge-CH2-CH3 portion of an IgG1 immunoglobulin using no more than ordinary skill and routine recombinant DNA and purification methods utilized in the art.

(iv) The Differences Between The August 1990 Prior Art and the Claimed Subject Matter

256. There are no differences between the prior art and the claimed subject matter. The prior art discloses all of the elements of the claimed subject matter. A person of ordinary skill in the art would have followed the clear motivation in the art to combine these elements with a reasonable expectation of success in doing so.

257. Combinations of the prior art that render the Asserted Claims of the Patents-in-Suit obvious are the following:

- Smith '760 patent in view of the Seed '262 publication;
- Smith '760 patent in view of Byrn 1990;
- Smith '760 patent in view of Watson 1990;
- Smith '760 patent in view of Karjalainen '827 publication;

- Smith '760 patent in view of Capon '964 patent in further view of Traunecker 1989; and
- Smith 1990 in view of Watson 1990.

(v) The Objective Indicia Support a Finding of Obviousness[23]

(a) Simultaneous Invention by Others

258. At least three research groups had, within a short time frame around August 1990, independently conceived of and developed fusion proteins comprising the extracellular region of the TNF receptor and the hinge-CH2-CH3 portion of an immunoglobulin.

259. Scientists at Immunex and Behringwerke had developed a fusion protein comprising a soluble p75 TNF receptor and hinge-CH2-CH3 domains of a human IgG1 prior to August 1990. This research eventually led to creation of etanercept at Immunex by November 1990. Etanercept was developed by scientists at Immunex, independent of any involvement of Plaintiff Roche.

260. The idea for the creation of a TNF receptor-IgG1 fusion protein was discussed in an October 1989 meeting between Immunex and Behringwerke. *See, e.g.*, DTX-111. At the time, Immunex had sequenced the full-length p75 TNF receptor and Behringwerke had experience expressing fusion proteins of receptors fused to the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin. With the DNA sequence for the p75 TNF receptor provided by Immunex, scientists at Behringwerke created the fusion protein in Germany.

261. By June 25, 1990, Behringwerke had sent a sample of the TNF receptor-IgG1 fusion protein in cell culture supernatant to Immunex in the United States. *See, e.g.*, DTX-87.

[23] Defendants object to Plaintiffs' statement of the disputed objective indicia to the extent that any of the objective indicia have not been properly raised or extend beyond the opinions offered by Plaintiffs' experts. Examples of the improper objective indicia include assertions of commercial success, licensing, and skepticism.

Testing by Immunex confirmed that the supernatant had TNF inhibitory activity and that the TNF receptor-IgG1 fusion protein did function as expected. *See, e.g.*, DTX-114. This fusion protein was comprised of a truncated portion of the extracellular region of the p75 TNF receptor (which was missing the last five amino acids of the extracellular region) fused to the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin via a three-amino acid linker.

262. On June 28, 1990, scientists at Behringwerke also filed German Patent Application No. P40 20 607.6 ("Lauffer DE '607 application") describing the construction of a TNF receptor fusion protein wherein the extracellular region of the TNF receptor is fused to the hinge-CH2-CH3 portion of a human IgG1 immunoglobulin. *See, e.g.*, DTX-105. The U.S. version of this patent application, U.S. Patent Application No. 07/581,703 ("Lauffer '703 application," DTX-102), was filed on September 13, 1990, with the scientists at Immunex later named as inventors on the application (DTX-103). Immunex and Behringwerke were reasonably diligent in the filing of the Lauffer '703 application in the United States on September 13, 1990.

263. Immunex and Behringwerke's TNF receptor-IgG1 fusion protein supports a finding that the Asserted Claims of the Patents-in-Suit would have been obvious. The only differences between Immunex and Behringwerke's TNF receptor-IgG1 fusion protein and the claimed fusion protein is that Immunex and Behringwerke's fusion protein lacks the five last amino acids of the extracellular region of the p75 TNF receptor and includes three-amino acid linker. A person of ordinary skill in the art would have been motivated to construct the TNF receptor-IgG1 fusion protein with the entire extracellular region of the p75 TNF receptor, without the three-amino acid linker.

264. The Lauffer '703 application supports a finding that the Asserted Claims of the Patents-in-Suit would have been obvious. The only difference between the TNF receptor-IgG1

fusion protein described in the Lauffer '703 application and the asserted claims is that the Patents-in-Suit specify that the TNF receptor is the p75 TNF receptor. A person of ordinary skill in the art would have been motivated to construct the Lauffer '703 TNF receptor-IgG1 fusion with the p75 TNF receptor.

265. The research by scientists at the University of Texas Southwestern Medical Center supports a finding that the Asserted Claims of the Patents-in-Suit would have been obvious. The UT Southwestern scientists had developed a TNF receptor-IgG heavy chain chimeric protein. Their fusion protein is described in Peppel 1991, which was submitted for publication in August 1991 and published in December 1991. DTX-26. The UT Southwestern scientists filed a patent application on April 2, 1992, which issued as U.S. Patent No. 5,447,851 ("Beutler '851 patent") on September 5, 1995. DTX-41. Immunex acquired the Beutler '851 patent.

266. The research by scientists at Genentech supports a finding that the Asserted Claims of the Patents-in-Suit would have been obvious. The Genentech scientists had developed a p55 TNF receptor-IgG1 protein. Their fusion protein is described in Ashkenazi 1991, which was received for review on June 13, 1991 and was published in December 1991. DTX-35.

267. The research at Immunex/Behringwerke, UT Southwestern, and Genentech demonstrate that scientists prior to and shortly after August 1990 had independently conceived and developed a fusion protein that fused an extracellular portion of a TNF receptor to the hinge-CH2-CH3 domain of an immunoglobulin.

(b) Plaintiffs' Objective Indicia Lack Nexus to the Claimed Invention

268. All of Plaintiffs' asserted objective indicia use etanercept as the embodiment of the claimed invention, and claim that etanercept and its effects are evidence that the Patents-in-

Suit are not obvious. But etanercept was developed by *Immunex*. The work of the named inventors at *Roche* on the p55 TNF receptor-IgG3 fusion protein was conducted independently from the work at Immunex on etanercept, and with no knowledge of what specific type of TNF receptor protein Immunex was developing. As such, Roche had no involvement in the discovery of etanercept. None of Plaintiffs' objective indicia, which all rely on *Immunex's* independent work in the development of etanercept, can show how Roche's work was inventive in light of the real-world research that was being conducted by scientists at around the same time.

(c) No Failure By Others

269. Plaintiffs have not shown that individuals others than the named inventors attempted to develop etanercept but failed to do so.

270. Individuals other than the named inventors at Roche—*i.e.*, the scientists at Immunex—had developed ENBREL® as an FDA-approved and commercial product. The named inventors at Roche had no involvement in the creation or development of Enbrel® into a commercial product. Immunex succeeded in the development of Enbrel® independent of any contribution from the named inventors at Roche.

271. Roche attempted to develop their p55 TNF receptor-IgG3 fusion protein but failed in clinical trials.

(d) No Unexpected Results, Proceeding Against Conventional Wisdom, or Skepticism

272. Plaintiffs have not shown that etanercept exhibits unexpected results.

273. Plaintiffs have not shown that etanercept surprisingly binds TNF with very high affinity relative to the soluble form of the p75 TNF receptor. The soluble form of the p75 TNF receptor can only bind the TNF trimer at only one binding site. But a person of ordinary skill in the art as of August 1990, would have expected that etanercept, as a dimeric fusion protein with

two soluble p75 TNF receptors, would bind the TNF trimer at two bindings sites. The enhanced binding of etanercept would have been expected when etanercept binds to more than one binding site on the same TNF trimer. This was known as the "avidity effect." As taught by the prior art, such a person would have been motivated to fuse the extracellular region of the p75 TNF receptor to the hinge-CH2-CH3 domain of a human IgG1 immunoglobulin based on the expected enhanced TNF binding activity of the dimeric fusion protein.

274. Plaintiffs have not shown that etanercept surprisingly does not form aggregates in the presence of TNF. Aggregates are higher-order complexes formed from the cross-linking of many receptors. Higher-order complexes may form when a receptor binds to more than one of its ligands, and each ligand cross-links a receptor to other receptors. A person of ordinary skill in the art as of August 1990 would not have expected etanercept to form these cross-links required to create higher-order complexes. Based on the avidity effect, a person of ordinary skill in the art would have expected that etanercept, as a dimeric fusion protein with two soluble p75 TNF receptors, would more strongly bind to two binding sites on the same TNF trimer as compared to binding to a single binding site on two different TNF trimers. When each etanercept binds to only one TNF trimer, there is no formation of cross-links between the etanercept molecules and no formation of higher-order complexes.

275. Plaintiffs have not shown that etanercept surprisingly exhibits little to no effector function activity of complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC). As of August 1990, a person of ordinary skill in the art would have known that initiation of CDC and ADCC activity requires the aggregation of antibodies into higher-order complexes. Etanercept's little to no effector function activity would have been expected in light of the expectation that etanercept would not form higher-order complexes in the

presence of TNF. Plaintiffs' comparison of the effector function activity of etanercept relative to the anti-TNF antibodies adalimumab and infliximab is improper, as these anti-TNF antibodies were undisputedly not available in the prior art.

276. Plaintiffs have not shown that the little to no effector function activity of etanercept is a beneficial property. Despite exhibiting some effector function activity, the anti-TNF antibodies adalimumab and infliximab are FDA-approved to treat each of the indications for which etanercept has been approved. Further, these anti-TNF antibodies have been FDA approved to treat Crohn's disease, which is an indication that has not been approved for etanercept. The efficacy of these anti-TNF antibodies to treat Crohn's disease has been associated with their effector function activity. Thus, Plaintiffs' allegations of surprising results have no nexus to the claimed invention.

277. Plaintiffs have not shown that the named inventors were proceeding against the conventional wisdom or that there was skepticism in the art.

278. Plaintiffs have not shown that the prior art taught away from developing a TNF receptor-IgG fusion protein. Plaintiffs assert that a person of ordinary skill in the art as of 1990 would have been concerned that etanercept would exhibit similar effector function activity to antibodies, and assert that this was expected to be disadvantageous in treating inflammatory diseases, such as rheumatoid arthritis. First, the prior art did not report any concerns of effector function activities from antibodies that target TNF. The prior art teaching anti-TNF antibodies and the chimeric TNF receptor antibody do not mention effector function activity. Second, the prior art taught administering other IgG1 fusion proteins for the treatment of inflammatory diseases, such as rheumatoid arthritis, without raising any concern of effector function activity.

279. Plaintiffs have not shown that the prior art expressed skepticism in light of questions that etanercept would raise immunogenicity issues due to its unnatural structure. Each of the p75 TNF receptor and IgG1 antibody are naturally produced in humans. Fusing the soluble p75 TNF receptor directly to the hinge-CH2-CH3 of an IgG1 antibody minimizes any immunogenicity issues.

280. Contrary to the opinions of Plaintiffs' experts, the research of scientists at Immunex, Behringwerke, UT Southwestern, and Genentech show that those actually working in the field at the time were not discouraged from or skeptical of developing a fusion protein comprising the extracellular region of the TNF receptor and the hinge-CH2-CH3 portion of an immunoglobulin. Thus, Plaintiffs' allegations of proceeding against conventional wisdom or skepticism have no nexus to the claimed invention or the real-world research activities.

(e) No Clinical Success, Commercial Success, Praise, Long-Felt Need, and Recognition By Others

281. Plaintiffs have not shown that etanercept monotherapy is clinically successful in treating rheumatoid arthritis, or that it has met a long-felt need. The treatment of rheumatoid arthritis with ENBREL® alone was not significantly better than the prior art treatment of methotrexate monotherapy or other treatments that had become available prior to approval of ENBREL®. ENBREL® monotherapy did not fulfill a long-felt need for the treatment of rheumatoid arthritis left by prior art therapies. Any clinical success was a result of a combination of etanercept and methotrexate, and thus lacks a sufficient nexus to the claimed invention.

282. Plaintiffs have not established that any praise or recognition of ENBREL® was directed to ENBREL® monotherapy, and thus have not established a sufficient nexus between the claimed invention and any such praise or recognition by others. Active marketing

contributed to the prescription of ENBREL® and other anti-TNF agents. ENBREL® is not effective in treating all TNF-mediated diseases, for which other anti-TNF agents have been approved. Specifically, the anti-TNF antibodies adalimumab and infliximab are approved by the FDA for each indications of etanercept, as well as for the treatment of Crohn's disease. Thus, any clinical success of etanercept in treating TNF-mediated diseases is not commensurate in scope with the invention as claimed and therefore lacks the requisite nexus.

283. Plaintiffs' allegations of clinical success is not probative of any recognized secondary consideration of nonobviousness. In addition, Plaintiffs have not shown why any clinical success years after the priority date would support the nonobviousness of the claimed invention.

284. To the extent that Plaintiffs are now asserting commercial success, Plaintiffs have not established that Enbrel is a commercial success. Plaintiffs' expert has not conducted a proper commercial success analysis, and Plaintiffs have not established any connection between the Patents-in-Suit and the commercial performance of Enbrel. For example, Plaintiffs' expert considers only one metric of commercial performance, a limited timeframe, and limited competitors. In addition, during its time on the market, Enbrel has been protected by numerous other patents, and the Patents-in-Suit did not issue until well after the time period addressed by Plaintiffs' expert.

(f) Copying Is Not Probative Evidence Of The Nonobviousness Of the Patents-in-Suit

285. Sandoz began its etanercept project no later than 2005—long before the Patents-in-Suit issued—and worked on it continuously until filing its aBLA in 2015. Consistent with the regulatory requirements that were in place in countries outside the U.S., Sandoz sequenced the commercial product Enbrel® and used the same primary amino acid sequence as the originator

for its product. At that time, the patents potentially relevant to etanercept included the Smith '760 and Jacobs '690 patents, which expired in 2012 and 2014, respectively. Sandoz intended to launch its product upon expiration of those patents.

286. On November 22, 2011, shortly before the Smith '760 patent was to expire, Amgen, which had acquired Immunex, issued a press release announcing that it had acquired the newly-issued '182 patent. Amgen announced that "[t]he patent describes and claims the fusion protein that is etanercept, and by statute, the '182 patent has a term of 17 years from today"—until November 2028. After Amgen issued its press release, Sandoz began to explore the possibility of "designing around" the Patents-in-Suit by modifying the amino acid sequence. The design-around project never entered *in vivo* testing and was discontinued in 2014 when it became clear that the same primary amino acid sequence as the originator would be necessary in order to obtain FDA approval as a biosimilar, similar to the requirements in other countries.

287. Sandoz filed a declaratory judgment action against Immunex, seeking a declaration that the Patents-in-Suit were invalid and/or not infringed, in 2013. Rather than admit that it was planning to sue Sandoz for patent infringement, Immunex filed a motion to dismiss, arguing that there was no subject matter jurisdiction over Sandoz's claims. The case was dismissed. *Sandoz Inc. v. Amgen Inc. et al.*, Case No. 2014-1693 (Fed. Cir. 2014).

288. Having worked on its product for approximately a decade, on July 30, 2015, Sandoz Inc. submitted a Section 351(k) application, aBLA No. 761042, to FDA, seeking authorization to market Erelzi® as a biosimilar version of Immunex's ENBREL® (etanercept) product in the United States. On August 30, 2016, FDA approved Defendants' Biosimilar

Etanercept for all the indications in which ENBREL® (etanercept) had been approved at that time.[24]

289. Sandoz filed and obtained FDA approval of its aBLA pursuant to the Biologics Price Competition and Innovation Act (BPCIA) enacted in 2010, which established an abbreviated pathway for regulatory approval of follow-on biological products that are "highly similar" to a previously approved biological drug product. Any copying by Sandoz of the amino acid sequence for etanercept reflects its efforts to meet the FDA standards for approval of biosimilar products under the BPCIA—not any nonobviousness of the Patents-in-Suit, which issued in 2011 and 2012. Thus, Plaintiffs' allegations of copying have no nexus to the claimed invention.

2. Plaintiffs' Statement

290. Defendants allege that each of the Asserted Claims is invalid as obvious under 35 U.S.C. § 103 based on one or more of six purported prior art combinations.[25]

291. Pursuant to the Amended Stipulation (D.I. 510 ¶ 3.b, *see also, supra*, § V.), Defendants have identified those six prior art combinations as follows:[26]

- U.S. Patent No. 5,395,760 ("Smith '760 patent") in view of European Patent Application Publication No. 0 325 262 ("Seed '262 publication");
- Smith '760 patent in view of Byrn RA *et al.*, *Biological properties of a CD4 immunoadhesin*, Nature 344:667-670 (1990) ("Byrn 1990");

[24] Sandoz subsequently amended its proposed label for Erelzi® to remove the indications for psoriatic arthritis (PsA) and plaque psoriasis (PsO), because these indications remained protected by the Finck patents until August 13, 2019.

[25] Joint Pretrial Report. D.I. 486.

[26] *See* June 5, 2018 Sandoz's Disclosure of Obviousness Combinations and Double Patenting Reference Families (attached as **Joint Exhibit 2**).

- Smith '760 patent in view of Watson SR *et al.*, *A homing receptor-IgG chimera as a probe for adhesive ligands of lymph node high endothelial venules*, Journal of Cell Biology 110:2221-2229 (1990) ("Watson 1990");
- Smith '760 patent in view of European Patent Application Publication No. 0 394 827 ("Karjalainen '827 publication");
- Smith '760 patent in view of U.S. Patent No. 5,116,964 ("Capon '964 patent") in further view of Traunecker A *et al.*, *Highly efficient neutralization of HIV with recombinant CD4-immunoglobulin molecules*, Nature 339:68-70 (1989) ("Traunecker 1989"); and
- Smith CA *et al.*, *A receptor for tumor necrosis factor defines an unusual family of cellular and viral proteins*, Science 248:1019-23 (1990) ("Smith 1990") in view of Watson 1990.

292. Plaintiffs dispute Sandoz's allegations of obviousness.

293. 35 U.S.C. § 103(a) states: "[a] patent may not be obtained … if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."

294. Obviousness is a question of law predicated on factual inquiries. The factual inquiries (the "*Graham* factors") include the following:[27]

(1) the level of ordinary skill in the art;

(2) the scope and content of the prior art;

(3) the differences between the claimed subject matter and the prior art; and

[27] *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

(4) objective indicia of non-obviousness, such as commercial success, long-felt but unsolved needs, failure of others, etc.

295. An alleged infringer cannot prove obviousness "merely by demonstrating that each of its elements was, independently, known in the prior art." *See KSR Int'l Co. v. Teleflex, Inc.,* 550 U.S. 398, 418 (2007). Instead, a party seeking to invalidate a patent as obvious "must demonstrate by clear and convincing evidence that a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1068-69 (Fed. Cir. 2012).

296. The use of hindsight is not permitted in an obviousness analysis. *KSR*, 550 U.S. at 421 (cautioning against "the distortion caused by hindsight bias" and "arguments reliant upon ex post reasoning"). In addition, the prior art must be considered "in its entirety, *i.e.*, as a whole," including the portions that suggest that the claimed invention would not have been obvious. *Panduit Corp v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568 (Fed. Cir. 1987); *see also Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1305 (Fed. Cir. 2011).

297. Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut the presumption of validity, Defendants bear the burden of proving invalidity by clear and convincing evidence. *Microsoft*, 564 U.S. at 110-14.

a. Plaintiffs' Statement of the Issues of Law to Be Litigated

298. Whether Defendants have proven, by clear and convincing evidence, that each of the Asserted Claims of the '182 patent is invalid for obviousness under 35 U.S.C. § 103 based on one or more of the six purported prior art combinations identified by Defendants.

299. Whether Defendants have proven, by clear and convincing evidence, that each of the Asserted Claims of the '522 patent is invalid for obviousness under 35 U.S.C. § 103 based on one or more of the six purported prior art combinations identified by Defendants.

b. Plaintiffs' Statement of the Issues of Fact to Be Litigated

300. Whether Defendants have proven, by clear and convincing evidence, the predicate factual underpinnings necessary to support their allegations that one or more of the six purported prior art combinations renders obvious the subject matter claimed in each of the Asserted Claims, including, but not limited to, the following:

Level of Skill in the Art[28]

301. Whether Defendants have proven, by clear and convincing evidence, that one working in the field as of August 31, 1990 and possessing ordinary skill in the art as of August 31, 1990 would have found the subject matter of the Asserted Claims to be obvious.

Scope and Content of the Prior Art

302. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated to develop, with a reasonable expectation of success, an agent that binds free, circulating TNF for use as:

- A therapeutic to treat disorders such as autoimmune disease and inflammation, amongst other agents and mechanisms that could have been explored to potentially treat these disorders and given that the physiological role of TNF in these disorders was unclear; or alternatively

[28] Plaintiffs propose the following level of skill in the art: A research scientist with an M.D. or Ph.D. and 1-2 years of relevant post-doctoral research experience in immunology, molecular biology, cellular biology, and/or biochemistry, with experience in DNA cloning, protein expression and purification, cell culture, and basic immunological structures and functions). *Compare, supra*, ¶ 250 (Defendants' proposal).

- A research reagent, despite the availability of other TNF-binding agents that existed in the art for such use.

303. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop an agent that binds free, circulating TNF for use as therapeutic or research reagent, would have been further motivated, with a reasonable expectation of success, to choose and select TNF-R, given that the physiological role of TNF-R was unclear, and despite the availability of other TNF-binding agents that existed in the art.

304. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop a TNF-R-based TNF binding agent for use as therapeutic or research reagent, would have been motivated, with a reasonable expectation of success, to choose p75 TNF-R, despite availability or disclosure of other TNF-binding agents that existed in the art, including but not limited to, other TNF-R molecules, such as p55 TNF-R.

305. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop a p75 TNF-R-based TNF binding agent for use as a therapeutic or a research reagent, would have looked to the Smith '760 patent or Smith 1990 patent for guidance.

306. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop a p75 TNF-R-based TNF binding agent for use as a therapeutic or a research reagent and looking to the Smith '760 patent or Smith 1990 for guidance, would have been further motivated, with a reasonable expectation of success, to choose the full extracellular region of p75 TNF-R, or the "recombinant chimeric antibody molecule" disclosed in the Smith '760 patent from among the various potential TNF-R based TNF-binding agents disclosed in the two references.

307. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop a p75 TNF-R-based TNF binding agent for use as therapeutic or research reagent, and looking to the Smith '760 patent or Smith 1990 for guidance, would have found the other potential TNF-R based TNF-binding agents disclosed in the two references to be unsuitable and thus would have sought further guidance from other relevant art.

308. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop an agent that binds free, circulating TNF for use as a therapeutic to treat disorders such as autoimmune disease and inflammation or use as a research reagent, would have considered as relevant to such development, art from fields relating to (i) cell-surface adhesion molecules designed to treat non-inflammatory conditions, such as HIV/AIDS, by eliciting the effector functions of antibodies and thereby provoking an inflammatory response (the Seed '262 publication, Byrn 1990, the Karjalainen '827 publication,[29] the Capon '964 patent and Traunecker 1989); or (ii) histochemical "probes" used to study the distribution of chemical structures affixed to the surface of cells (Watson 1990).

309. Whether Defendants have proven by clear and convincing evidence that an ordinary artisan, if motivated to develop a p75 TNF-R-based TNF binding agent for use as therapeutic or *in vitro* research reagent by choosing the "recombinant chimeric antibody molecule" disclosed in the Smith '760, and if further motivated to look to art outside the field for guidance, would have disregarded the teaching in the Smith '760 patent that such molecules have "unmodified constant region domains."

310. Whether Defendants have proven by clear and convincing evidence that the Karjalainen '827 publication, having been published after August 31, 1990, is prior art against

[29] The parties dispute whether the Karjalainen '827 publication is prior art.

the Asserted Claims.

Differences Between the Claimed Subject Matter and the Prior Art

311. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop the full extracellular region of p75 TNF-R or the "recombinant chimeric antibody molecule" in the Smith '760 patent for use as a therapeutic or research reagent, would have been motivated, with a reasonable expectation of success, to modify the structure of these proteins to "extend the half-life of the receptor, enhance the binding of the receptor to TNF, and permit use of standard [antibody-based] techniques to purify the receptor" by fusion to an immunoglobulin heavy chain constant region and make a fusion protein covered by the Asserted Claims given:

- The availability of other known methods and agents that could have been used address these issues if they were of concern to an ordinary artisan based on the prior art;
- The art taught that immunoglobulin fusion proteins were designed to treat AIDS by provoking an inflammatory response via the effector function of antibodies; and
- Teachings in the art that "[o]ne of the most important issues" confronting the use of immunoglobulin fusion proteins was "the extent of autoimmune damage."

312. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop the "recombinant chimeric antibody molecule" in the Smith '760 patent for use as a therapeutic or research reagent, would have been motivated, with a reasonable expectation of success, to modify the structure of this protein to "facilitate[] the expression and secretion" of the antibody given, for example, that the Smith '760 patent

expressly states that the chimeric antibody molecule should have "unmodified constant region domains."

313. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan, if motivated to develop the full extracellular region of p75 TNF-R or the "recombinant chimeric antibody molecule" in the Smith '760 patent for use as a therapeutic or research reagent, would have been motivated, with a reasonable expectation of success, to express either protein in Chinese hamster ovary cells.

314. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation of success, to combine the Smith '760 patent and the Seed '262 publication, and if so, whether Defendants have proven by clear and convincing evidence:

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

315. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation of success, to combine the Smith '760 patent and Byrn 1990, and if so, whether Defendants have proven by clear and convincing evidence:

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

316. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation of success, to combine the Smith '760 patent and Watson 1990, and if so, whether Defendants have proven by clear and convincing evidence:

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

317. Assuming the Karjalainen '827 publication is prior art (which the parties dispute, *see, supra*, ¶ 320, footnote 36), whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation of success, to combine the Smith '760 patent and the Karjalainen '827 publication, and if so, whether Defendants have proven by clear and convincing evidence;

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

318. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation, of success to combine the Smith '760 patent and the Capon '964 patent and Traunecker 1989, and if so, whether Defendants have proven by clear and convincing evidence:

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

319. Whether Defendants have proven by clear and convincing evidence that the ordinary artisan would have been motivated, with a reasonable expectation of success, to combine Smith 1990 and Watson 1990, and if so, whether Defendants have proven by clear and convincing evidence:

- That the combination discloses each and every element of any of the Asserted Claims; and
- That the combination would have motivated the ordinary artisan, with a reasonable expectation of success, to (i) make a fusion protein that meets each and every element of the Asserted Claims of the '182 patent, and (ii) carry out a process for making a fusion protein that meets each and every element of the Asserted Claims of the '522 patent.

Objective Indicia of Non-Obviousness

320. Whether, once established by Plaintiffs, Defendants have rebutted, by clear and convincing evidence, the objective indicia supporting nonobviousness, including but not limited to the following:

- Clinical success that provides evidence of commercial success, given the widespread and rapid adoption of ENBREL® in the United States;[30]
- Praise in light of laudatory statements regarding ENBREL® by numerous physicians and patients;
- Long-felt, but unmet need, and the failure of others, in light of the advantages of ENBREL® in, for example, patients that previously could not be successfully

[30] Defendants argue that "allegations of clinical success is not probative of any recognized secondary consideration of nonobviousness." *See, supra*, ¶ 295. Defendants presented a version of this argument in their *Daubert* motion against Drs. Fleischmann and Vellturo, D.I. 521, which Plaintiffs addressed, D.I. 533. The Court has denied Defendants' motion. D.I. 572 at 9. Defendants also allege that "Plaintiffs' expert has not conducted a proper commercial success analysis." *See, supra*, ¶ 296. Defendants are incorrect on this point. Both Drs. Fleischmann and Vellturo addressed commercial success as demonstrated by clinical success. Courts have upheld this type of analysis. *See, e.g.*, *Pfizer Inc. v. Teva Pharm U.S.A. Inc.*, 882 F. Supp. 2d 643, 671 (D. Del. 2012), *aff'd*, 555 F. App'x 961 (Fed. Cir. 2014) (addressing commercial success as objective indicium and stating "the court finds credible the testimony of the plaintiff's expert ... who explained that Lyrica has the largest share of prescriptions for branded products to treat diabetic peripheral neuropathy and postherpetic neuralgia combined in the United States and is one of the two leading branded products prescribed for the treatment of fibromyalgia"); *Janssen Pharm., Inc. v. Watson Labs, Inc.*, 2012 WL 3990221, *18 (D.N.J. Sep. 11, 2012) (using, in part, prescriptions written as evidence of commercial success).

treated with prior art therapies, and the fact that others, among other things, attempted to develop TNF binding proteins for the treatment of inflammatory disorders, but failed;

- Skepticism in light of questions that etanercept would raise immunogenicity issues due to its unnatural structure;
- Licensing by others of the patented technology;
- Unexpected results, such as the fact that etanercept exhibits little to no effector function activity, binds TNF with very high affinity relative to soluble forms of p75 TNF-R, and does not form aggregates with TNF are unexpected properties, given, for example, that the physical and structural factors that give rise to these advantages were not known in August 1990 and remain unclear even today; and
- Copying, given Sandoz's intentional use of the identical amino acid sequence of the etanercept drug substance found in ENBREL®, and decision to use the same the CHO host cell expression system used to make the etanercept drug substance found in ENBREL® after identifying "design around" variants of etanercept that Sandoz recognized could have been approved by FDA.[31]

[31] Defendants argue that copying is "not probative" of nonobviousness (*see, supra*, ¶¶ 240, 297-301) for the same reasons that they sought to strike the testimony of Immunex and AML's expert, Dr. Jones. D.I. 521; D.I. 532; D.I 539. The Court declined to exclude Dr. Jones's testimony. D.I. 572. Again, Defendants ignore case law from the Federal Circuit holding that, even in the "Hatch-Waxman" context, copying can be a relevant objective indicia where, as here, copying is not required for regulatory approval. *E.g.*, *Merck Sharp & Dohme Corp. v. Hospira, Inc.*, 874 F.3d 724, 731 (Fed. Cir. 2017) ("[The Hatch-Waxman Act] does not . . . require the generic manufacturer to copy the . . . process of ***manufacturing*** the drug" (emphasis original)). Plaintiffs also dispute Defendants' characterization of their efforts to develop Defendants' Biosimilar Etanercept. Plaintiffs further object to these statements as they seek to introduce facts relating to arguments that the Court has ordered Defendants are precluded from making at trial, such as arguments relating to the prosecution laches defense that Defendants have withdrawn. D.I. 597.

321. Whether Defendants have rebutted, by clear and convincing evidence, the presumption that that there is a nexus between etanercept and the Asserted Claims given that the Asserted Claims cover etanercept.

322. Whether Defendants have proven, by clear and convincing evidence, objective indicia supporting obviousness, including but not limited to:

- Whether Defendants have proven, by clear and convincing evidence, any facts that qualify as "simultaneous invention," including, for example, by proving whether and when multiple other groups made etanercept and whether, if they did so, whether the work was made independently of the claimed inventions and whether the level of skill in the art and state of the art was the same at the time of the alleged "simultaneous invention" as it was as of the August 31, 1990 invention date of the Asserted Claims;[32] and
- Whether Defendants have proven, by clear and convincing evidence, how any facts tending to show "simultaneous invention," if proven, may be used as indicia supporting obviousness in light of the requirement that the motivation to combine and reasonable expectation of success must be based on the prior art and the knowledge of the ordinary artisan at the time of the invention; and
- Whether Defendants have proven, by clear and convincing evidence, how any facts tending to show "simultaneous invention," if proven, may be used as indicia supporting obviousness in light of the Patent Act's provision for "interference" proceedings that recognize that multiple groups may simultaneously seek patents on the same or similar subject matter. *E.g., Lindemann Maschinenfabrik GMBH*

[32] The Patents-in-Suit claim priority to the Brockhaus '707 application, which was published on March 20, 1991.

v. Am. Hoist & Derrick Co., 730 F.2d 1452, 1460 (Fed. Cir. 1984) ("Because the statute, 35 U.S.C. § 135, (establishing and governing interference practice) recognizes the possibility of near simultaneous invention by two or more equally talented inventors working independently, that occurrence may or may not be an indication of obviousness when considered in light of all the circumstances.").

c. Response to Defendant's Statement of Contested Facts

323. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section above. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

D. Written Description (35 U.S.C. § 112)

1. Defendants' Statement

324. A patent's specification "shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." 35 U.S.C. § 112, ¶ 1.

325. Thus, the first paragraph of § 112 contains two separate requirements: a "written description" and "enablement." *See Ariad Pharm., Inc., v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

326. Whether a specification satisfies the written description requirement is a question of fact. *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 729 (Fed. Cir. 2014).

327. For a patent specification to incorporate "another document by reference [*e.g.*, a patent application], the incorporating document must identify the incorporated document with

detailed particularity, clearly indicating the specific material for incorporation." *Kyocera Wireless Corp. v. Int'l Trade Comm'n*, 545 F.3d 1340, 1352 (Fed. Cir. 2008).

328. To comply with the written description requirement, a patentee must describe "the invention, with all its claimed limitations" as of the filing date. *ICU Med., Inc. v Alaris Med. Sys., Inc.,* 558 F.3d 1368, 1379 (Fed. Cir. 2009) (citation omitted). A specification contains adequate written description if "the description . . . clearly allow[s] persons of ordinary skill in the art to recognize that the inventor invented what is claimed," and "had possession of the claimed subject matter as of the filing date." *Ariad Pharm.*, 598 F.3d at 1351 (quotation and alterations omitted).

329. "[T]he hallmark of written description is disclosure," and "the test requires an objective inquiry into the four corners of the specification" to determine whether it "show[s] that the inventor actually invented the invention claimed." *Id.* The Federal Circuit has "repeatedly stated that actual 'possession' or reduction to practice outside of the specification is not enough"; "the specification itself … must demonstrate possession." *Id.* at 1352. A "description that merely renders the invention obvious does not satisfy the requirement." *Id.*

330. A "mere wish or plan" for obtaining the claimed invention is not an adequate written description. *Centocor Ortho Biotech, Inc. v. Abbott Labs.,* 636 F.3d 1341, 1348 (Fed. Cir. 2011).

331. The original disclosure must provide adequate direction which reasonably would lead persons skilled in the art to "single out" the invention from the various alternatives discussed in the disclosure. *See id.*; *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1325-26 (Fed. Cir. 2000); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996); *In re Ruschig*, 54 C.C.P.A. 1551, 379 F.2d 990, 995 (C.C.P.A. 1967). In particular, "where a patentee adds

claims during prosecution that....were not included in the original priority application, courts require a detailed description and identification of the later-claimed invention in the original disclosure, particularly where the specification discloses numerous possibilities with scant guidance on which to select." *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336 (Fed. Cir. 2013). Even if the specification "provides formal textual support for each individual limitation recited in the claims" it must describe the actual, functioning species that falls within the claims. *Id.* at 1349.

332. "When a patent claims a genus using functional language to define a desired result, the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299 (Fed. Cir. 2014) (citation omitted). Thus, when a specification only describes one type of structurally similar proteins which are not representative of the full scope of the genus, there is no written description support for proteins that differ significantly from those described. *Id.* at 1300. "A court may rely on post-priority-date evidence to determine if a patent discloses a representative number of species." *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1373 (Fed. Cir. 2017) (citation omitted).

333. Merely describing one embodiment of a claimed invention does not necessarily satisfy the written description requirement; instead, description of a "single embodiment would support [] a generic claim only if the specification would reasonably convey to a person of skill in the art that [the inventor] had possession of the claimed subject matter." *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1346 (Fed. Cir. 2005). If "the specification ... fail[s]

to demonstrate that the patentee possessed the full scope of the invention recited in [a] claim" at the time of filing, it "provides inadequate support for the claim under section 112." *Id.* at 1345.

334. A "mere wish or plan" for obtaining the claimed invention is not an adequate written description. *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2011).

a. Defendants' Statement of the Issues of Law to be Litigated

335. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for lack of written description?

b. Defendants' Statement of the Issues of Fact to be Litigated

336. Whether the Asserted Claims of the Patents-in-Suit are invalid for lack of written description because the specification as of September 1990 did not describe the invention, with all its claimed limitations?

337. Whether the Asserted Claims of the Patents-in-Suit are invalid for lack of written description because the specification as of September 1990 did not describe the extracellular region of the insoluble human TNF receptor with an apparent molecular weight of about 75 kilodaltons (*i.e.* the full p75 extracellular region)?

338. Whether the Asserted Claims of the Patents-in-Suit are invalid for lack of written description because the specification as of September 1990 does not describe all the domains of the constant region of a human IgG1 immunoglobulin heavy chain other than the first domain of the constant region (*i.e.* the hinge-CH2-CH3 region of a human IgG/IgG1)?

339. Whether the Asserted Claims of the Patents-in-Suit are invalid for lack of written description because the specification as of September 1990 does not describe a fusion protein combining the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1?

340. Whether the Asserted Claims of the Patents-in-Suit are invalid for lack of written description because the specification as of September 1990 does not describe a fusion protein combining the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1 that specifically binds human TNF?

c. Defendants' Statement of the Contested Facts

341. Each of the Asserted Claims of the Patents-in-Suit are invalid for failure to meet the written description requirement of 35 U.S.C. § 112, ¶ 1.

342. The Asserted Claims of the Patents-in-Suit are generally directed to a fusion protein comprised of the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1, wherein the fusion protein specifically binds human TNF. A person of ordinary skill in the art reading the specification would not have understood that the Roche inventors had invented and possessed a fusion protein comprising the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1 as of September 1990.

343. The Roche inventors filed the U.S. application leading to the Patents-in-Suit in September 1990. The Roche inventors were employed by Plaintiff Roche. The Roche inventors were not employed by Plaintiffs Immunex at the time of filing the application leading to the Patents-in-Suit. From the late 1980s through at least the late 1990s, the Roche inventors worked on a p55 TNF receptor-IgG3 fusion protein. Roche's p55 TNF receptor-IgG3 fusion protein failed in clinical trials. The Roche inventors did not take any p75 TNF receptor-IgG1 fusion protein to clinical trials. Also during the late 1980s and through the 1990s, Immunex was working on a fusion protein comprised of the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1, later approved to be marketed as ENBREL® starting in 1998.

344. The specification as of September 1990 describes the invention as "TNF-binding proteins…containing the amino acid sequence depicted in FIG. 1…or in FIG. 4…." *See, e.g.,*

'182 patent, DTX-1, at col. 3, ll. 4-11. The specification as of September 1990 provides in Figure 1 a full p55 TNF receptor. The specification provides in Figure 4 a fragment of a purported p75 TNF receptor with mutations. The protein described in Figure 4 is a different protein than the full p75 extracellular region.

345. The specification as of September 1990 describes as the invention the Figure 4 protein—not a protein with the full p75 extracellular region. The specification as of September 1990 does not describe the full p75 extracellular region to one of ordinary skill in the art. As compared to the actual sequence of 235 amino acids comprising the full p75 extracellular region, the Figure 4 fragment deleted amino acids 1-70 of the full p75 extracellular region, contains three amino acid mutations, and has one extra amino acid. Although it was not known in 1990 because the specification does not report any TNF binding data, it is now known that the amino acid deletions result in significant consequence, including likely affecting the Figure 4 protein's ability to specifically bind TNF.

346. The specification describes the Figure 4 fragment as "preferred" and a smaller fragment of Figure 4 containing one less amino acid as "especially preferred". *See, e.g.,* '182 patent, DTX-1, at col. 5, ll. 35-40. The specification discloses that despite repeated sequencing, the inventors obtained only the "preferred" Figure 4 fragment, and not the sequence of the full p75 TNF receptor. The Roche inventors chose to describe only the sequence of the Figure 4 fragment and fragments thereof as their invention in the specification. The Roche inventors did not describe the sequence of the full p75 extracellular region in the specification.

347. The specification as of September 1990 does not incorporate by reference the full p75 TNF extracellular region described in the scientific literature. It directs a person of ordinary skill in the art to the sequence disclosed in Smith 1990 only as an example of a deletion of one

amino acid in the Figure 4 fragment. *See, e.g.,* '182 patent, DTX-1, at col. 5, ll. 22-24. A deletion of one amino acid in the Figure 4 fragment would not include the full extracellular region of the p75 TNF receptor.

348. None of the examples in the specification as of September 1990 provide any instruction for making a fusion protein comprised of the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1. The specification provides in Example 11 a cloning procedure that mentions the TNF receptor sequence for only the p55 TNF receptor—not the p75 TNF receptor. The method of Example 11 cannot be used to obtain a fusion protein comprised of the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1, like etanercept.

349. A p55 TNF receptor-IgG3 fusion protein has structurally distinct component parts as compared to a p75 TNF receptor-IgG1 fusion protein. First, the p55 and p75 TNF receptors were shown to be structurally distinct with different amino acid sequences. Second, the IgG3 antibody has a unique structure and activity among the different subtypes of the human IgG isotype, including a having a characteristic repeated hinge region (62 amino acids, compared to the 13-15 amino acids in the IgG1 hinge, depending on the definition).

350. In June 2004, Roche and Immunex entered into an "Accord & Satisfaction Agreement" that transferred to Immunex all substantive ownership rights to the Patents-in-Suit. *See* 2004 Accord & Satisfaction Agreement, DTX-357. Thereafter, Immunex took over prosecution of the applications that led to the Patents-in-Suit.

351. Immunex materially amended the specification and changed the scope of the pending claims in an attempt to purportedly cover etanercept following transfer of control of the prosecution of the application to Immunex. For example, in November 2006, Immunex amended

the specification to reference the plasmid PTA 7942. Plasmid PTA 7942 was unavailable at the timing of filing the patent application. Plasmid PTA 7942 was only deposited on October 17, 2006 with the American Type Culture Collection. Inconsistencies in the amino acid sequences of Plasmid PTA 7942 and the Figure 4 fragment reflect that the Figure 4 fragment encodes a different protein than that encoded by Plasmid PTA 7942.

352. The specification as of September 1990 does not describe the hinge-CH2-CH3 region of a human IgG/IgG1.

353. The parties stipulated that the claimed phrase "all the domains of the constant region of a human IgG1 immunoglobulin heavy chain other than the first domain of the constant region" has its "plain and ordinary meaning: '-hinge-CH2-CH3' region of a human [IgG/IgG1].'" D.I. 144 at 1.

354. The specification as of September 1990 does not mention the term "hinge". A person of ordinary skill in the art in September 1990 would have understood that a hinge region of a human IgG/IgG1 has more than one plain and ordinary meaning and that the Patents-in-Suit lack written description for which hinge to use.

355. The specification does not describe a fusion protein combining the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1, or that the named inventors possessed such a fusion protein or had devised a procedure for making such a fusion protein. A person of ordinary skill in the art would not have understood that the named inventors had described and shown possession of the claimed the fusion protein based upon the examples of the Patents-in-Suit.

356. The specification does not teach a fusion protein combining the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1 that specifically binds TNF.

2. Plaintiffs' Statement

357. Defendants allege that each of the Asserted Claims is invalid for failure to satisfy the written description requirement under 35 U.S.C. § 112.[33]

358. Plaintiffs dispute Defendants' allegations of lack of written description.

359. 35 U.S.C. § 112 states a patent's specification must "contain a written description of the invention."

360. Written description requires "an objective inquiry into the four corners of the specification from the perspective" of an ordinary artisan to determine if it "describe[s] an invention understandable to that skilled artisan and show[s] that the inventor actually invented the invention claimed." *Ariad Pharm. Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

361. To satisfy the written description requirement, the specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.*

362. For inventions relating to biological materials, written description may be established by a deposit of a sample of the biological material with an independent depository accessible to the public, and identification of the deposited material in the patent specification at any time prior to the issuance of the patent. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 965-67 (Fed. Cir. 2002); *see also* 37 C.F.R. § 1.804(a) (". . . an original deposit [of

[33] Joint Pretrial Report. D.I. 486.

biological material] . . . may be made . . . subject to § 1.809, during pendency of the application for patent.").

363. The identification of deposited material in a patent specification can be made at any time prior to the issuance of the patent and does not constitute new matter. *In re Lundak*, 773 F.2d 1216, 1218-20, 1223 (Fed. Cir. 1985); *see also* 37 C.F.R. § 1.804(a) (". . . an original deposit [of biological material] . . . may be made . . . subject to § 1.809, during pendency of the application for patent.").

364. "[E]xamples are not necessary to support the adequacy of a written description" and "there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006); *see also Ariad*, 598 F.3d at 1352 ("the written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement").

365. Where "accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences . . . , satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences." *Falko-Gunter Falkner*, 448 F.3d at 1368; *see also Capon v. Eshhar et al.*, 418 F.3d 1349, 1361 (Fed. Cir. 2005) (written description requirement does not impose "a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field").

366. Whether a specification satisfies the written description requirement is a question of fact. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991); *see also Ariad*, 598 F.3d at 1351.

367. Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut the presumption of validity, Defendants bear the burden of proving invalidity by clear and convincing evidence. *Microsoft*, 564 U.S. at 110-14.

a. Plaintiffs' Statement of the Issues of Fact to Be Litigated

368. Whether Defendants have proven by clear and convincing evidence that the specification of the Patents-in-Suit fails to convey to an ordinary artisan that the inventors possessed the subject matter of the Asserted Claims under 35 U.S.C. § 112 at the time of the invention (*i.e.*, August 31, 1990) given, for example, the following:

- The specification describes fusion proteins which consist of a soluble fragment of non-soluble TNF binding proteins and an immunoglobulin fragment, *i.e.*, "all domains except the first domain of the constant region of the heavy chain";
- The p75 TNF-R sequences disclosed in the specification provide identifying information sufficient to show that the inventors possessed the entire p75 TNF-R protein, and DNA encoding the entire protein;
- The specification describes routine methods for identifying the entire amino acid and DNA sequence of the p75 TNF-R, which if followed, would have resulted in the same sequences disclosed in the literature;
- The specification lists the Smith 1990 reference as a publication disclosing sequences of the p75 TNF-R protein;

- Amino acid and nucleotide sequences disclosed in the specification identify the p75 TNF-R protein as the same protein disclosed in the prior art Smith 1990 reference (which disclosed these sequences);
- The Patent Office allowed an amendment to the specification identifying ATCC Accession No. PTA 7942, a publicly available biological deposit, which includes a plasmid with a cDNA insert that encodes the p75 TNF-R amino acid sequence;
- The DNA and amino acid sequences of the heavy chain constant region of IgG immunoglobulins, including IgG1 and IgG3, were known in the art;
- The specification describes pCD4-Hγ1 and pCD4-Hγ3 as publicly available vectors that can be used to make the fusion protein of the Asserted Claims;
- Soluble forms of TNF-R were known in the art to bind TNF with high affinity and the extracellular binding domain of p-75 TNF-R was known in the art; and
- Recombinant DNA technology was a mature field and recombinant DNA techniques were routine.

b. Response to Defendant's Statement of Contested Facts

369. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section above. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

E. Enablement (35 U.S.C. § 112)

1. Defendants' Statement

370. The second requirement of § 112 is "enablement." *See Ariad*, 598 F.3d at 1351.

371. Enablement is a question of law, with factual inquiries underlying the determination. *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 940 (Fed. Cir. 2010).

372. To meet the enablement requirement, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012).

373. "Enablement serves the dual function in the patent system of ensuring adequate disclosure of the claimed invention and of preventing claims broader than the disclosed invention." *Magsil Corp.*, 687 F.3d at 1380-1381.

374. To determine if the experimentation necessary is undue, courts consider: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

375. Where the prior art alone establishes enablement of claimed subject matter, "[a] patent cannot both be non-obvious and enabled." *In re '318 Patent Infringement Litig.*, 578 F. Supp. 2d 711, 736 (D. Del. 2008), aff'd, 583 F.3d 1317 (Fed. Cir. 2009). A patent "cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification." *ALZA Corp.*, 603 F.3d at 941.

376. Conversely, "a description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of § 112, ¶ 1." *Regents of Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1567 (Fed. Cir. 1997) (emphasis omitted).

377. Patent protection is granted "in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." *Genentech, Inc. v. Novo Nordisk A/S,* 108 F. 3d 1361, 1366 (Fed. Cir. 1997). "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." *Id.* Thus, "when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art." *Id.*

a. Defendants' Statement of the Issues of Law to be Litigated

378. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the Patents-in-Suit are invalid for lack of enablement?

b. Defendants' Statement of the Issues of Fact to be Litigated

379. Whether the Asserted Claims of the Patents-in-Suit are invalid for failure to meet the enablement requirement of 35 U.S.C. § 112, ¶ 1.

c. Defendants' Statement of the Contested Facts

380. Each of the Asserted Claims of the Patents-in-Suit are invalid for failure to meet the enablement requirement of 35 U.S.C. § 112, ¶ 1.

381. The Roche inventors filed the application leading to the Patents-in-Suit in 1990. The Roche inventors were employed by Plaintiff Roche. The Roche inventors were not employed by Plaintiffs Immunex and Amgen at the time of filing the application leading to the Patents-in-Suit. The Roche inventors worked on a p55 TNF receptor-IgG3 fusion protein, which failed in clinical trials.

382. The Asserted Claims of the Patents-in-Suit are generally directed to a fusion protein comprised of the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1, wherein the fusion protein specifically binds human TNF.

383. The specification does not allow persons of ordinary skill in the art to recognize that the Roche inventors invented and possessed a fusion protein comprised of the full p75 extracellular region and hinge-CH2-CH3 region of a human IgG/IgG1 as of September 1990.

384. The specification does not teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation as of September 1990.

385. The specification fails to describe, among other things, (1) the full p75 extracellular region, (2) the hinge-CH2-CH3 region of a human IgG/IgG1, (3) a fusion protein combining the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG, and (4) such a fusion protein that specifically binds TNF.

386. Without disclosure in the specification of the specific constituent parts for making a fusion protein combining the full p75 extracellular region and the hinge-CH2-CH3 region of a human IgG/IgG1 or of how the process for making a fusion protein can be carried out, undue experimentation is required to make and use the full scope of the claimed invention.

387. The specification does not supply the purported novel aspects of the claimed invention. The failure to provide an enabling disclosure cannot be rectified by asserting that all the disclosure related to the claimed invention is within the skill of the art.

2. Plaintiffs' Statement

388. Defendants allege that each of the Asserted Claims is invalid for lack of enablement under 35 U.S.C. § 112.[34]

[34] Joint Pretrial Report. D.I. 486.

389. Plaintiffs dispute Defendants' allegations of lack of enablement.

390. 35 U.S.C. § 112 states a patent specification must contain a written description "of the manner and process of making and using [the invention], in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ."

391. To satisfy the enablement requirement, a patent specification must teach one of ordinary skill in the art "'how to make and use the full scope of the claimed invention without undue experimentation.'" *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1378 (Fed. Cir. 2009) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)).

392. "A claim is sufficiently enabled even if 'a considerable amount of experimentation' is necessary, so long as the experimentation 'is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 684 (Fed. Cir. 2015) (quoting *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).

393. Enablement is a question of law based on underlying facts. *See In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991).

394. Facts relevant to the enablement requirement (the "*Wands* factors") include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Wands*, 858 F.2d at 737.

395. Issued patents are presumed valid. *See* 35 U.S.C. § 282(a). To rebut the presumption of validity, Defendants bear the burden of proving invalidity by clear and convincing evidence. *Microsoft*, 564 U.S. at 110-14.

a. Plaintiffs' Statement of the Issues of Law to Be Litigated

396. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the '182 patent are invalid because the specification fails to enable the claimed subject matter.

397. Whether Defendants have proven by clear and convincing evidence that the Asserted Claims of the '522 patent are invalid because the specification fails to enable the claimed subject matter.

b. Plaintiffs' Statement of the Issues of Fact to Be Litigated

398. Whether Defendants have proven by clear and convincing evidence that the specifications of the Patents-in-Suit would not have enabled an ordinary artisan to make and use the subject matter of each of the Asserted Claims without undue experimentation, given, for example, the following:

- The narrow breadth of the claims, which cover a specific fusion protein consisting of the extracellular region of p75 TNF-R fused to the "-hinge-CH2-CH3 region of a human IgG immunoglobulin";
- The disclosure provided in the specification, the state of the art, and the general knowledge in the art. *See* Written Description, Issues of Fact to be Litigated, *supra*, § VII.E.2; and
- The level of skill in the art as recognized by Defendants and Plaintiffs. *See, supra*, § VII.D.2.b, footnote 35.

c. Response to Defendant's Statement of Contested Facts

399. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section above. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

F. Anticipation and Obviousness of Claims 35 and 36 of the '182 Patent (35 U.S.C. §§ 102, 103)

1. Defendants' Statement

400. "[A] patent application is entitled to the benefit of the filing date of an earlier filed application only if the disclosure of the earlier application provides support for the claims of the later application, as required by 35 U.S.C. § 112." *In re Chu*, 66 F.3d 292, 297 (Fed. Cir. 1995). Section 112 written description requires that the application "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter *as of the filing date*." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (emphasis added); *see also Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1571-72 (Fed. Cir. 1997).

401. "When the applicant adds a claim or otherwise amends his specification after the original filing date . . . the new claims or other added material must find support in the original specification." *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. Gen. Elec. Co.*, 264 F.3d 1111, 1118 (Fed. Cir. 2001).

402. When presented with invalidating prior art, the patentee has "the burden of going forward with evidence . . . that it is not prior art because the asserted claim is entitled to the benefit of a filing date prior to the alleged prior art." *Tech Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1327 (Fed. Cir. 2008). To claim the benefit of an earlier application, the patentee must "show not

only the existence of the earlier application, but why the written description in the earlier application supports the claim" before the burden of production shifts to the accused infringer. *Id.*

403. A person shall be entitled to a patent unless —

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or . . .

35 U.S.C. § 102(a), (b).

404. "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a).

a. Defendants' Statement of the Issues of Law to be Litigated

405. Whether Plaintiffs have shown that claims 35 and 36 of the '182 patent are entitled to claim priority to the European Patent Application No. 90116707 ("the Brockhaus '707 application") filed on August 31, 1990, when those claims recite the amino acid sequence of the plasmid PTA 7942, which was not referenced in the patent specification until a November 2006 amendment?

406. Whether Defendants have proven by clear and convincing evidence that claims 35 and 36 of the '182 patent are invalid as anticipated or obvious to a person of ordinary skill in the art as of November 2006 pursuant to 35 U.S.C. §§ 102, 103?

b. Defendants' Statement of the Issues of Fact to be Litigated

407. Whether the Brockhaus '707 application provides written description support for the claimed plasmid PTA 7942?

408. Whether prior to the November 2006 amendment to the patent specification adding reference to the claimed plasmid PTA 7942, any of the applications from which the '182 patent derives provide written description support for the plasmid?

409. Whether the prior art as of November 2006 anticipates or renders obvious each of claims 35 and 36 of the '182 patent?

c. Defendants' Statement of the Contested Facts

410. The Brockhaus '707 application does not describe the amino acid sequence encoded by the claimed plasmid PTA 7942. None of the other pre-November 2006 applications from which the '182 patent derives provide written description support for the claimed plasmid PTA 7942.

411. Asserted claims 35 and 36 of the '182 patent would have been anticipated by the prior art as of November 2006, and/or would have been obvious to a person of ordinary skill in the art in November 2006.

412. The Jacobs '690 patent (DTX-17) issued on February 25, 1997. The patent describes in Example 2 the construction and expression of an exemplary soluble human TNFR/Fc fusion protein and provides in Figure 1 a schematic representation of the etanercept molecule. Other developments in the prior art between August 1990 and November 2006 include the approval of ENBREL® in the United States on November 2, 1998, the sale of ENBREL® in the United States for more than one year prior to November 2006, and the publication of studies describing the administration of ENBREL® and its uses.

413. The prior art describing etanercept anticipates claims 35 and 36 of the '182 patent, which claim etanercept and a pharmaceutical composition comprising etanercept. A person of ordinary skill in the art would have also found the Asserted Claims of the '182 patent obvious in light of etanercept. The objective evidence does not support a finding that asserted claims 35 and 36 of the '182 patent is nonobvious over the prior art describing etanercept.

2. Plaintiffs' Statement

414. Defendants allege that claims 35 and 36 of the '182 patent are invalid as anticipated by the prior art or obvious in view of the prior art.

415. Plaintiffs dispute Defendants' allegations of anticipation and obviousness.

416. A claim is entitled to the benefit of the filing date of an earlier application if the earlier application includes a written description of the subject matter of the claim and the earlier application enables the claimed subject matter. *Frazer v. Schlegel*, 498 F.3d 1283, 1287 (Fed. Cir. 2007); *Martek,* 579 F.3d at 1369.

417. The earlier application "need not describe the claimed subject matter in precisely the same terms as found in the claims at issue." *Martek,* 579 F.3d at 1369. Instead, the test for the sufficiency of the support in the earlier filed application is "whether the disclosure of the application relied upon 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.'" *Id.*

418. To satisfy the enablement requirement, a patent specification must teach one of ordinary skill in the art "'how to make and use the full scope of the claimed invention without undue experimentation.'" *Id.* at 1378.

419. Subject matter supported by the original disclosure of a patent application may be added to the specification by an amendment after the application is filed. *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. G.E.*, 264 F.3d 1111, 1118-19 (Fed Cir. 2001). If a

proposed amendment adds subject matter that is not supported by the original disclosure, it adds "new matter" to the specification and claims covering the amended subject matter are rejected by the Patent Office for failing to satisfy the written description requirement of 35 U.S.C. § 112. *TurboCare* at 1119-20; *see also In re Rasmussen*, 650 F.2d 1212, 1214-15 (CCPA 1981).

420. The question of whether an amendment adds new matter to the disclosure is essentially the same as the question of whether the original disclosure provides written description support for the added subject matter, which is a question of fact. *Rasmussen*, 650 F.2d at 1214-15; *Ariad*, 598 F.3d at 1351.

421. The identification of deposited material in a patent specification is not new matter if made prior to the issuance of the patent. *Lundak*, 773 F.2d at 1223; *see also* 37 C.F.R. § 1.804(a) (". . . an original deposit [of biological material] . . . may be made . . . subject to § 1.809, during pendency of the application for patent.").

422. An alleged infringer seeking to invalidate a patent based on the argument that the claims of the patent are not entitled to the effective filing date of the earliest filed application for which the patent claims priority must prove that the earlier filed application does not provide written description support and enable the subject matter of the claims by clear and convincing evidence. *See, e.g.*, *Martek*, 579 F.3d at 1369, n. 3.

423. Further, the Federal Circuit has held that "in the context of a validity challenge based on new matter, the fact that the [Patent Office] has allowed an amendment…is entitled to an especially weighty presumption of correctness." *Commonwealth Scientific & Indus. Research Org. v. Buffalo Tech. (USA), Inc.*, 542 F.3d 1363, 1380 (Fed. Cir. 2008) (citing *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1574-5 (Fed. Cir. 2002)).

424. The ultimate determination of whether a specific claim is entitled to the effective filing date of an earlier application is a question of law. *E.I. du Pont de Nemours & Co. v. MacDermid Printing Sols., L.L.C.*, 525 F.3d 1353, 1359 (Fed. Cir. 2008).

a. Plaintiffs' Statement of the Issues of Law to Be Litigated

425. Whether Defendants have proven by clear and convincing evidence that claims 35 and 36 of the '182 patent are not entitled to claim the benefit of an August 31, 1990 filing date of European Patent Application No. 90116707.

426. Whether Defendants have proven by clear and convincing evidence that the Patent Office's determination that the amendment to the specification to identify biological deposit ATCC No. PTA 7942 recited in claims 35 and 36 of the '182 patent prior to the issuance of the '182 patent was improper by proving by clear and convincing evidence that the Patent Office erred in determining that the amendment was supported by the original disclosure and therefore did not add new matter.

b. Plaintiffs' Statement of the Issues of Fact to Be Litigated

427. Whether Defendants have proven by clear and convincing evidence that claims 35 and 36 of the '182 patent are invalid as anticipated by the prior art given that these claims are entitled the benefit of the August 31, 1990 filing date of European Patent Application No. 90116707.

428. Whether Defendants have proven by clear and convincing evidence that the specification of the Patents-in-Suit fails to convey to an ordinary artisan that the inventors possessed the subject matter of claims 35 and 36 of the '182 patent at the time of the August 31, 1990 filing of European Patent Application No. 90116707 given, for example:

- The disclosure of the application (*see, supra*, § VII.E.2 (Plaintiffs' Statement regarding Written Description); and

- The Patent Office's determination that the amendment to the specification to identify biological deposit ATCC No. PTA 7942 recited in claims 35 and 36 of the '182 patent was supported by the original disclosure and therefore did not constitute new matter and was proper.

c. Response to Defendant's Statement of Contested Facts

429. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section above. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the relevant facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

G. Exceptional Case (35 U.S.C. § 285)

1. Plaintiffs' Statement

430. 35 U.S.C. § 285 states that the "court in exceptional cases may award reasonable attorney fees to the prevailing party."

431. An "exceptional" case under 35 U.S.C. § 285 is "one that stands out from others with respect to the substantive strength of a party's litigating position (considering both the governing law and the facts of the case) or the unreasonable manner in which the case was litigated." *Octane Fitness, LLC v. ICON Health & Fitness, Inc.*, 134 S. Ct. 1749, 1756 (2014).

432. The determination of whether a case is exceptional is "generally . . . 'rooted in factual determinations.'" *Highmark Inc. v. Allcare Health Mgmt. Sys., Inc.*, 134 S.Ct. 1744, 1748-49 (2014).

433. Factors supporting a finding that a case is exceptional, such as deliberate copying of an invention, need not be pled for the Court to consider the evidence at trial. *Barry v.*

Medtronic, Inc., 250 F. Supp. 3d 107, 114-115 (E.D. Tex. Apr. 20, 2017); *see also Read Corp. v. Portec, Inc.*, 970 F.2d 816, 826-27 (Fed. Cir. 1992).

434. Plaintiffs must show by a preponderance of the evidence that a case is exceptional. *Octane Fitness*, 134 S. Ct. at 1758.

a. Plaintiffs' Statement of the Issues of Law to Be Litigated

435. Whether Plaintiffs can prove, by a preponderance of the evidence, facts at trial relevant to the question of whether this case is exceptional—which Plaintiffs have pled in their Complaint (*see* D.I. 1 at 35).

b. Plaintiffs' Statement of the Issues of Fact to Be Litigated

436. Whether Plaintiffs have proven by a preponderance of the evidence that this is an exceptional case such that the court should award attorneys' fees under 35 U.S.C. § 285, given Defendants' conduct during litigation (*e.g.*, improper privilege redactions), assertion of meritless defenses such as prosecution laches and invalidity under 35 U.S.C. 102(g), and deliberate copying of the subject matter of the Asserted Claims following attempts to "design around" the Patents-in-Suit.

c. Response to Defendant's Statement of Contested Facts

437. Plaintiffs object to Defendants' "Statement of Contested Facts" in the section below. Rather than identifying disputed factual questions, Defendants' statement does nothing more than provide a summary of Defendants' position (in paragraph form) based on a misleading and selective portrayal of the facts. In addition, many of the facts that Defendants characterize as not disputed are, in fact, disputed.

2. Defendants' Statement

438. "The court in exceptional cases may award reasonable attorney fees to the prevailing party." 35 U.S.C. § 285.

439. A case may be found to be "exceptional" under 35 U.S.C. § 285 for any one or more of the following reasons: lack of substantive strength of litigating position, unreasonable conduct, or subjective bad faith. *Octane Fitness, LLC v. ICON Health & Fitness, Inc.*, 134 S. Ct. 1749, 1756-57 (2014).

440. To show that a party's litigating position warrants an "exceptional case" finding, it is not sufficient to rely exclusively on the fact that the position did not ultimately prevail. *See id.* at 1753 (noting § 285 attorney fees are not "a penalty for failure to win a patent infringement suit"). Further, the filing of an application to the FDA for approval of a biological product is an artificial act of infringement under 35 U.S.C. § 271(e)(2)(C) that, alone, cannot give rise to an award for attorney's fees. *See Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1674-75 (2017); *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1350-51 (Fed. Cir. 2004). Instead, "a district court may award fees in the rare case in which a party's unreasonable conduct—while not necessarily independently sanctionable—is nonetheless so 'exceptional' as to justify an award of fees." *Id.* at 1757.

441. The absence of inequitable conduct before the PTO, vexatious, unjustified, and otherwise bad faith litigation, a frivolous suit, or willful infringement weighs against an exceptional case finding. *AstraZeneca AB v. Aurobindo Pharma Ltd.*, 232 F. Supp. 3d 636 (D. Del. 2017); *Brigham & Women's Hosp., Inc. v. Perrigo Co.*, No. CV 13-11640-RWZ, 2017 WL 1496916, at *5 (D. Mass. Apr. 24, 2017) (denying plaintiff's motion for attorney's fees, because defendant's defense of the suit was neither frivolous nor vexatious); *Tyco Healthcare Grp. LP v. Mut. Pharm. Co., Inc.*, No. 07CV1299SRCCLW, 2016 WL 3965201, at *1 (D.N.J. July 22, 2016) (denying Defendants' motion for attorney's fees because Plaintiff did not engage in sham litigation and it is inappropriate to find a case exceptional based on a "battle of the experts").

a. Defendants' Statement of the Issues of Law to be Litigated

442. Whether the mere filing of an abbreviated Biologics License Application (aBLA) can support a finding of exceptional case?

b. Defendants' Statement of the Issues of Fact to be Litigated

443. Whether Plaintiffs' actions in this litigation have given rise to an exceptional case such that the court should award Defendants' attorneys' fees under 35 U.S.C. § 285?

444. Whether Defendants' actions in this litigation have given rise to an exceptional case such that the court should award Plaintiffs' attorneys' fees under 35 U.S.C. § 285?

c. Defendants' Statement of the Contested Facts

445. Defendants' actions in defending this litigation do not demonstrate an exceptional case. For example, Defendants' litigating position does not lack substantive strength, and Defendants have not engaged in unreasonable conduct or subjective bad faith.

446. Nor does Sandoz's "copying" of Enbrel demonstrate an exceptional case. Sandoz began its etanercept project no later than 2005 and worked on it continuously until filing its aBLA in 2015. The Patents-in-Suit did not issue until 2011 and 2012, despite having been pending with the PTO since 1995.

VIII. REMEDIES

447. On June 7, 2017, the parties agreed to postpone discovery on remedies, including a permanent injunction, until after trial on the merits.[35]

[35] June 7, 2017 e-mail from Julia Mano Johnson to Marc Haefner.

IX. WITNESSES

A. Plaintiffs' Witnesses

Fact Witnesses

1. **Hansruedi Loetscher, Ph.D. (live):** Dr. Loetscher is an inventor of the '182 and '522 patents. He received an undergraduate degree in Biochemistry at the Swiss Federal Institute of Technology, which is a specialized school for high achieving technical students in Switzerland. He also received a Ph.D. from the Swiss Federal Institute of Technology in 1981. He then completed post-doctoral research at the University of Oregon.

2. Dr. Loetscher recently retired from F. Hoffmann-La Roche AG's facility in Basel, Switzerland, where he worked from 1984 through 2016. Prior to his retirement, Dr. Loetscher served as the Global Head of Neuroscience Discovery and as the Section Head of Neurodegeneration and Regeneration, where he led efforts to find treatments for Parkinson's and Alzheimer's diseases. In his over 30-year scientific career, Dr. Loetscher authored over 70 scientific publications, including in *Nature*, the *Journal of Biological Chemistry*, *Drug Discovery Today*, the *Journal of Immunology*, and the *Journal of Investigative Dermatology*.

3. Dr. Loetscher is expected to testify about, among other things, the research and development of the subject matter of the '182 patent and the '522 patent.

4. **Werner Lesslauer, Ph.D. (by deposition):** Dr. Lesslauer is an inventor of the '182 and '522 patents. He received a Medical Degree from the University of Basel in 1962. He received a Ph.D. in Physical Chemistry from the University of Basel in 1966. His post-doctoral work focused on the biophysical study of biological membranes. In 1979, he presented a written manuscript and trial lecture at the University of Bern, where he received a *venia docendi*, a qualification to become a *Privatdozent*, or Associate Professor. After teaching and conducting research in biology and biochemistry at the University of Bern for several years, he began work

as a Staff Scientist at F. Hoffinan-La Roche AG in 1987. He worked at Roche in Basel, Switzerland for 12 years, where he retired as a Vice-Director of Research. Following his retirement, Dr. Lesslauer took a visiting faculty position in the Department of Epidemiology and Public Health at Yale University School of Medicine. He has authored over 100 publications, including in *Cell*, *Nature*, the *Journal of Biological Chemistry*, the *Journal of Immunology*, and the *Journal of Experimental Medicine*.

5. Dr. Lesslauer is expected to testify about, among other things, the research and development of the subject matter of the '182 patent and the '522 patent.

6. **Laura Hamill (live):** Ms. Hamill is currently Amgen's Senior Vice President of U.S. Domestic Operations. She has worked at Amgen since 2002. She previously worked at Immunex, where she was Vice President in the Inflammation Division and where she was responsible for all aspects of ENBREL® (etanercept), except sales of ENBREL®. Ms. Hamill is expected to testify about, among other things, ENBREL® and various commercial and marketing issues relating to ENBREL®.

7. **Stuart Watt (live):** Mr. Watt has worked at Amgen for over 25 years. He started as a patent attorney in Amgen's legal department in 1992, and currently serves as Amgen's Vice President of Law and Intellectual Property Officer. Mr. Watt is expected to testify about, among other things, Immunex's licensing of the Patents-in-Suit. Mr. Watt will also serve as Immunex and AML's corporate representative during trial.

8. **Dr. Taruna Arora (by deposition):** Dr. Arora is a former scientist at Amgen. She started as a Research Scientist in 2003, was promoted to Senior Scientist in 2005, and was promoted to Principal Scientist in 2008. She left Amgen in 2011. Plaintiffs will call Dr. Arora to, among other things, provide a foundation for, and to authenticate, certain documents,

including laboratory notebooks and the declaration she submitted during prosecution of the Patents-in-Suit.

9. **Dr. Tadahiko Kohno (by deposition):** Dr. Kohno is a former scientist at Amgen and Synergen Inc. ("Synergen"). He worked as a scientist at Synergen from 1985 until Amgen acquired Synergen in 1994. He continued working as a scientist at Amgen until he retired as Scientific Director in 2007. Plaintiffs will call Dr. Kohno to provide testimony regarding, among other things, ENBREL® (etanercept) and research related to the p55 TNF receptor protein.

10. **Dr. Christine Berndt (by deposition):** Dr. Berndt is the Global Project Leader for the Defendants' Biosimilar Etanercept program. Plaintiffs will call Dr. Berndt as an adverse witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept and various commercial, business, and marketing issues relating to Defendants' Biosimilar Etanercept.

11. **Dr. Peter Alliger (by deposition):** Dr. Alliger is a Technical Project Manager at Sandoz. Plaintiffs will call Dr. Alliger as an adverse witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept, Defendants' awareness of the Patents-in-Suit, and Defendants' research and development efforts.

12. **Dr. Cindy Cao, Ph.D. (by deposition):** Dr. Cao is a former Executive Director for Regulatory Affairs Biopharmaceuticals at Sandoz. Plaintiffs will call Dr. Cao as an adverse witness to testify, *inter alia*, about Defendants' Biosimilar Etanercept and various regulatory issues relating to Defendants' Biosimilar Etanercept.

13. **Dr. Mark McCamish (live or by deposition):** Dr. McCamish is the former Global Head of Biopharmaceutical Development at Sandoz. Plaintiffs will call Dr. McCamish as an adverse witness to testify about, *inter alia*, Defendants' efforts to "design around" the '182 patent and the '522 patent, Defendants' Biosimilar Etanercept, Defendants' awareness of the

Patents-in-Suit, Defendants' research and development efforts, and various regulatory, business, commercial, and marketing issues relating to Defendants' Biosimilar Etanercept.

14. **Dr. Zhengyu Liu (by deposition):** Dr. Liu is the former U.S. Regulatory Lead of the U.S. Biopharmaceutical Regulatory Affairs Group at Sandoz. Plaintiffs will call Dr. Liu as an adverse witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept and various regulatory issues relating to Defendants' Biosimilar Etanercept.

15. **Dr. Martin Schiestl (by deposition):** Dr. Schiestl is the Chief Science Officer at Sandoz. Plaintiffs will call Dr. Schiestl as an adverse witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept and Defendants' research and development efforts.

16. **Dr. Gautier Sala (live):** Dr. Sala is Executive Director, Biopharmaceutical Regulatory Affairs at Sandoz. Plaintiffs will call Dr. Sala as an adverse witness to testify about, *inter alia*, Defendants' awareness of the Patents-in-Suit, and Defendants' research and development efforts directed to designing around the Patents-in-Suit. Plaintiffs object to Defendants assertion that Dr. Sala may "testify regarding the research and development of the product that is the subject of Sandoz's aBLA No. 761042." Dr. Sala was designated as a Rule 30(b)(6) witness by Sandoz solely on topics related to the design-around efforts during discovery; he was not subject to a Rule 30(b)(1) deposition. If the Court allows Defendants to call Dr. Sala to "testify regarding the research and development of the product that is the subject of Sandoz's aBLA No. 761042," Plaintiffs reserve the right to likewise call Dr. Sala on the same subject matter.

17. **Gregory Oakes (by deposition):** Mr. Oakes is a former Vice President and Head of Biopharmaceuticals North America at Sandoz Inc. Plaintiffs will call Mr. Oakes as an adverse

witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept and various business, commercial, and marketing issues relating to Defendants' Biosimilar Etanercept.

18. **Dr. Ruediger Jankowsky (by deposition):** Dr. Jankowsky is a former Global Program Leader for Biopharmaceutical Development for Defendants. Plaintiffs will call Dr. Jankowsky as an adverse witness to testify about, *inter alia*, Defendants' Biosimilar Etanercept and Defendants' research and development efforts.

Expert Witnesses[36]

19. **Roy Fleischmann, M.D. (live):** Professor Fleischmann is an expert in the field of rheumatic diseases and disorders. He received an A.B. in Zoology from Columbia College in New York City in 1964. He received an M.D. from State University of New York, Downstate Medical Center in 1969. He is the Founder and Co-Medical Director of the Metroplex Clinical Research Center in Dallas, Texas, and a Clinical Professor in the Department of Internal Medicine at the University of Texas, Southwestern Medical Center at Dallas. His career has spanned over 40 years and has involved numerous clinical trials in the field of rheumatology, including rheumatoid arthritis. Metroplex Clinical Research Center was one of the sites where clinical trials with ENBREL® (etanercept) were conducted, and Metroplex continues to be involved in the investigation and development of drugs for treatment of rheumatoid arthritis.

20. Professor Fleischmann has published over 200 articles in peer-reviewed journals in the field of rheumatology. He is currently the editor in chief of *Rheumatology and Therapy*, and serves on the editorial boards of *Expert Opinion on Drug Safety*, *Rheumatology* (Oxford), and *Annals of the Rheumatic Diseases*. Professor Fleischmann serves as a journal referee for 20

[36] Plaintiffs reserve the right to have Dr. Kittendorf's expert report, or portions thereof, read into evidence. *See, infra*, § X.

publications, including *Arthritis and Rheumatology*, *Arthritis Care and Research*, the *Journal of Rheumatology*, and *Nature Rheumatology*. He has held numerous leadership positions, including serving as President of Texas Rheumatism Society and serving on the Board of Directors of the Arthritis Foundation, North Central Chapter. He has been voted one of *D Magazine*'s "Best Doctors in Dallas" and one of *Texas Monthly*'s "Best Doctors in Texas." He is also a Master of the American College of Rheumatology, an honor he received based on his achievements in drug development and teaching.

21. Professor Fleischmann is expected to provide expert testimony concerning, *inter alia,* objective indicia of non-obviousness, including the clinical success of ENBREL® (etanercept), praise and recognition received by ENBREL®, and the long-felt medical need met by ENBREL®.

22. **Randolph Wall, Ph.D. (live):** Professor Wall is an expert in the fields of immunology, molecular biology, and antibody engineering. He received a B.A. in Botany and Bacteriology from the University of South Florida in 1965 and a Ph.D. in Microbiology from Indiana University in 1970. He is currently Distinguished Professor in the Department of Microbiology, Immunology, and Molecular Genetics in The Molecular Biology Institute, University of California at Los Angeles (UCLA) and the David Geffen School of Medicine at UCLA. Professor Wall's career spans over 45 years and has included many important discoveries and pioneering projects. As a post-doctoral researcher, for example, Dr. Wall discovered the fundamental properties involved in the generation and function of messenger RNA (mRNAs), an achievement essential for the development of recombinant cloning of cDNA from mRNA. He co-founded Ingene, a biotechnology company that was one of the first to generate genetically engineered "chimeric" antibodies.

23. Professor Wall has taught courses in many subjects, including molecular biology, immunology, and virology. He has published over 100 articles, reviews, and book chapters. He has served on the editorial boards of the *Journal of Immunology* and *Molecular Cellular Biology*. He has also served on panels and committees for the National Science Foundation, National Cancer Institute, and National Institute of General Medical Sciences of the National Institutes of Health.

24. Professor Wall is expected to provide expert testimony concerning, ***inter alia***, the level of ordinary skill in the art, claim construction, Defendants' infringement of the '522 patent and the following validity issues related to the '182 patent and the '522 patent: non-obviousness, lack of obviousness-type double patenting, and the adequacy of the disclosures of the '182 patent and the '522 patent.

25. **Graham Jones, Ph.D. (by expert report and deposition):** Professor Jones is an expert in the fields of analytical chemistry, biopharmaceutical drug research, and regulatory science. He received a B.Sc. in Chemistry, with high honors, from the University of Liverpool in 1986. He received a Ph.D. in Organic Chemistry from the Imperial College of Science Technology and Medicine in London in 1989, where he was awarded the Cancer Research Foundation Fellowship. He was a NATO Fellow at Harvard University from 1989-1991, where he worked under E.J. Corey, the recipient of the Nobel Prize in Chemistry in 1990. Professor Jones also received a D.Sc. from the University of Liverpool in 2006 for career contributions in the field of chemistry.

26. Professor Jones is a Professor of Medicine and Director of Research Collaborations at Tufts University Medical Center in Boston, Massachusetts, where he also serves as the Associate Director of the Clinical and Translational Science Institute. He

previously served as the Executive Director of the Biopharmaceutical Analysis Training Laboratory (BATL), a research facility formed in collaboration with the FDA for the purposes of advanced training and outreach in areas such as biological drug characterization, biological product regulation, and the development of training programs for FDA employees in the broad areas of biotechnology and analytical chemistry. He also established a Professional Science Master's program in Regulatory Science at Northeastern University. Following the enactment of the BPCIA, Professor Jones testified before the FDA in a panel hearing that helped the Agency establish its practices and policies in implementing the BPCIA, as reflected in the FDA's "Guidance for Industry" publications on demonstrating biosimilarity.

27. Professor Jones has authored over 150 publications in the areas of analytical chemistry, biopharmaceutical drug research, and regulatory science. He has also served as an editor for the *International Journal of Medicinal Chemistry* and *Advances in DNA Sequence Specific Agents*, and a reviewer for the *Journal of the American Chemical Society*, *Nature*, and *Science*. He has also served as an advisor to the American Chemical Society, and the National Green Chemistry Initiative. He also advises several governmental agencies, including the National Science Foundation, National Institutes of Health, and the Department of Defense. He has given dozens of invited lectures in the U.S. and internationally.

28. Professor Jones is expected to provide expert testimony concerning, *inter alia*, the FDA's practices and policies regarding demonstrating biosimilarity, and the science underlying the FDA's policies, as relevant to Sandoz's copying of Immunex's etanercept as an objective indicium of non-obviousness.

29. **Warner Greene, M.D., Ph.D. (live):** Professor Greene is an expert in the fields of molecular biology, immunology, and virology. He received a B.A. in Biology, with Great

Distinction, from Stanford University in 1971. He obtained an M.D. and Ph.D., with honors, from Washington University School of Medicine in St. Louis in 1977. He is the Founder and Director of the Gladstone Institute of Virology and Immunology in San Francisco, and is also the Nick and Sue Hellman Distinguished Professor of Translational Medicine at the University of California, San Francisco. He has over 40 years of experience as a biomedical researcher, including study of tumor necrosis factor signaling pathways and the characterization of cytokine receptors.

30. Professor Greene has been recognized as one of the 100 most cited scientists in the world by the Institute for Scientific Information. He has served on the editorial boards of several journals, including the *Journal of Immunology*, *Cytokine*, *Molecular Biology of the Cell*, and the *Journal of Clinical Investigation*. He has also served as a reviewer for numerous journals, including *Nature*, *Science*, *Immunity*, and the *Journal of Experimental Medicine*. He has held numerous leadership positions, including Vice President of the American Society for Clinical Investigation and President of the Association of American Physicians. He has given dozens of honorary lectures in the U.S. and internationally. Professor Greene's work has been honored by the American Federation for Clinical Research and the American Rheumatism Association.

31. Professor Greene is expected to provide expert testimony concerning, *inter alia*, the work of others attempting to create a TNF receptor fusion protein at or around the time of the invention, the lack of obviousness-type double patenting, and the unexpected properties of ENBREL® (etanercept), as an objective indicium of non-obviousness.

32. **Christopher Vellturo, Ph.D. (live):** Dr. Vellturo is the Founder and President of Quantitative Economic Solutions, LLC, a microeconomic consulting firm, located in Boston,

Massachusetts. He is an expert in the field of economics, including in the areas of industrial organization and econometrics. He received a Sc.B. in Applied Mathematics and Economics, magna cum laude and Phi Beta Kappa, from Brown University in 1983. He also received a Ph.D. in Economics from the Massachusetts Institute of Technology in 1989.

33. Dr. Vellturo has published on many topics, including market definition, price discrimination, merger and acquisition-related efficiencies, and differentiated product analysis. His research has appeared in academic journals, including *Antitrust*, the *Antitrust Law Journal*, and the *Journal of Economics and Management*. He has served as a journal referee for American Economic Review and the Rand Journal of Economics. He was honored with the M.I.T. Departmental Fellowship in 1986 and the Bradley Fellowship in Public Economics for 1987-1989.

34. Dr. Vellturo is expected to provide expert testimony concerning, *inter alia*, the demand for and success of ENBREL® (etanercept) and its nexus to the Asserted Claims, as objective indicia of non-obviousness.

35. **James Naismith, Ph.D. (live):** Professor Naismith is an expert in the fields of structural biology, chemistry, and biochemistry. He received a B.Sc. in Chemistry, with First Class Honors, from the University of Edinburgh in 1989. Following graduate studies in Structural Biology and Chemistry, Dr. Naismith received a Ph.D. in 1992 from the University of Manchester, where he was awarded the Hibbert Prize for his dissertation. He is currently the Professor of Structural Biology at the University of Oxford in the United Kingdom. His post-doctoral research at the Howard Hughes Medical Institute in Dallas, Texas focused on the structure and function of the proteins involved in tumor necrosis factor signaling.

36. Professor Naismith is also the Director of the Research Complex at Harwell, a multidisciplinary research center in Oxford, England that provides facilities for researchers to undertake new and cutting-edge research in both the life and physical sciences and the interface between these two fields. His over 20-year research career has focused on the structure and function of proteins. He was involved in research to elucidate the three-dimensional structure of the p55 TNF receptor protein, and was the first to publish a solved structure for the p55 TNF receptor extracellular domain.

37. He has served as an editor or on the editorial board of the *Journal of Biological Chemistry*, the *Journal of Molecular Biology*, and the *Biochemical Journal*. He has also served as a journal referee for *Science*, *Nature*, *Biochemistry*, and the *Journal of the American Chemical Society*. His research has been recognized by several respected scientific organizations. Among other recognitions, he has been named a fellow of the Royal Society (UK) for Improving Natural Knowledge, the world's oldest scientific institution. He is also a fellow of the Royal Society of Edinburgh, the Academy Medical Sciences (UK), the American Association for the Advancement of Science, and the European Molecular Biology Organization. He has received numerous awards for his research accomplishments, including from the Royal Society of Chemistry, the Biochemical Society, and the Chinese Academy of Science. He is the only person to win both the Corday-Morgan Medal for contributions to chemistry and the Colworth Medal for contributions to biochemistry.

38. Professor Naismith is expected to provide expert testimony concerning, *inter alia*, the adequacy of the disclosures of the '182 patent and the '522 patent and the unexpected properties of ENBREL® (etanercept), as an objective indicia of non-obviousness.

39. **Stephen G. Kunin, J.D. (live):** Mr. Kunin is the former Deputy Commissioner for Patent Examination Policy in the Office of the Commissioner for Patents in the United States Patent Office (USPTO). He is an expert in USPTO policies, practices, and procedures. He received a B.S. in Electrical Engineering, with honors, from Washington University in 1970. He received a J.D., with honors, from the National Law Center of the George Washington University in 1975. He is currently a partner at the law firm of Maier & Maier PLLC, and he has served as the Intellectual Property L.L.M. and J.D. Programs Director at the George Mason School of Law, where he taught patent law and intellectual property courses.

40. Mr. Kunin has over 47 years of experience in the field of intellectual property and patents, including over 30 years at the USPTO. His career at the USPTO began in 1970 as a patent agent and culminated in ten years of service as the Deputy Commissioner for Patent Examination Policy. In his role as Deputy Commissioner, Mr. Kunin was involved in establishing and developing USPTO patent policies and patent examiner guidelines, as set forth in the USPTO's Manual of Patent Examining Procedure (MPEP). He also oversaw the operation of the Office of Patent Legal Administration, the Patent Cooperation Treaty Legal Administration, and the Office of Petitions.

41. Mr. Kunin has authored over 20 publications on patent law, and he has served on the editorial board of the *AIPLA Quarterly Law Journal*. He has received many awards during his career, including a USPTO Career Achievement Award, the Vice President's Reinventing Government Hammer Award, four Gold Medal Awards for Outstanding Service from the Department of Commerce, four Silver Medal Awards for Outstanding Service, and a Bronze Medal Award for Outstanding Service. In 2001, he was named one of the most influential people in intellectual property law by *Intellectual Property Today*. In 2002, *Global Counsel*

named him one of the most inspiring regulators in federal government. Since entering private practice, Mr. Kunin has been ranked several times by Chambers U.S.A. as one of the nation's top intellectual property lawyers.

42. Mr. Kunin is expected to provide expert testimony concerning, *inter alia*, the USPTO's practices and procedures regarding (i) the application of the "safe harbor" provision of 35 U.S.C. § 121, as relevant to the issue of obviousness-type double patenting, and (ii) the "two-way test" for patentable distinctness.

****

Plaintiffs may offer testimony live or by deposition from the above-listed witnesses, as identified above. For witnesses that will be testifying by expert report, the report will be admitted into evidence. Plaintiffs also reserve the right to have all or parts of the report read into evidence. Plaintiffs reserve the right to call additional witnesses (who are not presently identifiable) as may be necessary, on reasonable notice to the opposing party. In the event Plaintiffs seek to call a substitute witness, Plaintiffs agree to make an application to the Court to amend the Joint Final Pretrial Order.

Plaintiffs reserve the right to call and/or cross-examine any of Defendants' witnesses, including by counter-designation of deposition testimony.

Plaintiffs also reserve the right to call, either live or by deposition: (a) additional witnesses to provide foundational testimony should any party contest the authenticity or admissibility of any material proffered at trial; (b) substitute witnesses for any identified witnesses whose employment or other relationship with Plaintiffs changes such that he or she is no longer able, available or willing to testify on Plaintiffs' behalf at trial; and/or (c) additional witnesses to respond to issues raised after the submission of this list.

Plaintiffs expressly reserve the right to further modify, supplement and/or amend this Final Pretrial Order and attachments in light of issues that remain open and until entry of the Final Pretrial Order.

B. Defendants' Objections to Plaintiffs' Witnesses

Defendants object to the presentation of deposition testimony for any witness that is within Plaintiffs' control and current employees. As set forth in Defendants' *Daubert* motion, Defendants object to the proposed testimony of Plaintiffs' experts Dr. Graham Jones and Dr. Christopher Vellturo. *See* D.I. 520; D.I. 532; D.I. 533; D.I. 539.

With respect to all live witnesses, Sandoz reserves all objections as to relevance and admissibility.

Defendants object to Plaintiffs' proposal to have parts of expert reports read into evidence under Fed. R. Evid. 106 for lack of completeness and under Fed. R. Evid. 401 and 403 for unfair prejudice, confusion, misleading, undue delay, wasting time, and needlessly presenting cumulative evidence. Defendants further object as Plaintiffs have not disclosed which portions of which expert reports that it seeks to have read into evidence.

To the extent that Plaintiffs are allowed to have parts of an expert report read into evidence, Defendants reserve the right to counter-designate other portions of the report or the expert's testimony that should be read into evidence for completeness. Defendants further reserve the right to have all or parts of the report read into evidence for witnesses that will be testifying by expert report.

C. Defendants' Witnesses

Sandoz identifies the following witnesses whom it may call live or by deposition at trial:

Expert Witnesses

43. **Carl P. Blobel, M.D., Ph.D. (live):** Dr. Blobel is a Professor of Medicine and of Physiology and Biophysics at the Weil Medical College of Cornell University in New York, NY, as well as the Virginia F. and William R. Salomon Chair in Musculoskeletal Research and Director of the Arthritis and Tissue Degeneration Program at the Hospital for Special Surgery in New York, NY. Dr. Blobel is expected to offer testimony in accordance with his expert reports. Such testimony concerns issues relating to invalidity of the asserted claims of the '182 and '522 patents, including for obviousness under 35 U.S.C. § 103 and obviousness-type double patenting.

44. **Daniel Capon, Ph.D. (live):** Dr. Capon is a scientist with 37 years of experience in the field of biotechnology, including at Genentech, Inc., Cell Genesys, Inc., Xenotech, Inc., and ViroLogic, Inc. Dr. Capon is expected to offer testimony in accordance with his expert reports. Such testimony concerns issues relating to invalidity of the asserted claims of the '182 and '522 patents, including for lack of adequate written description and enablement under 35 U.S.C. § 112.

45. **Mary Kuntz Crow, M.D. (live):** Dr. Crow is a rheumatologist and the Physician-in-Chief, Chair of the Department of Medicine, and Chief of the Division of Rheumatology at the Hospital for Special Surgery in New York, NY. Dr. Crow is expected to offer testimony in accordance with her expert report. Such testimony concerns issues relating to the asserted objective indicia of nonobviousness of the '182 and '522 patents, including what Plaintiffs characterize as the alleged "clinical success," previously unmet need, and industry praise of Enbrel® and the nexus of these objective indicia to the asserted claims of the '182 and '522 patents.

46. **Nicholas P. Godici (live):** Mr. Godici is an independent consultant with over 44 years of experience in the patent field, including at the U.S. Patent and Trademark Office and at the intellectual property law firm of Birch, Stewart, Kolasch & Birch LLP. Mr. Godici is expected to offer testimony in accordance with his expert report. Such testimony concerns issues relating to invalidity of the asserted claims of the '182 and '522 patents, including for obviousness-type double patenting.

47. **Jeffrey D. Kittendorf, Ph.D. (by expert report and deposition)[37]:** Dr. Kittendorf is a Research Assistant Scientist at the University of Michigan Life Sciences Institute. Dr. Kittendorf submitted a declaration regarding DNA sequencing of plasmid DNA samples. Dr. Kittendorf is expected to testify regarding the subject matter of his declaration.

48. **DeForest McDuff, Ph.D. (live):** Dr. McDuff is a Partner at Insight Economics. Dr. McDuff is expected to offer testimony in accordance with his expert reports. Such testimony concerns issues relating to the asserted objective indicia of nonobviousness of the '182 and '522 patents, including what Plaintiffs characterize as the alleged "clinical success" of Enbrel®.

49. **Arne Skerra, Ph.D. (live):** Dr. Skerra is the Chair of Biological Chemistry at the Technical University of Munich, Center of Life Sciences at Weihenstephan, Freising, Germany. Dr. Skerra is expected to offer testimony in accordance with his expert report. Such testimony concerns issues relating to the asserted objective indicia of nonobviousness of the '182 and '522 patents, including the alleged unexpected results of Enbrel®.

[37] Defendants propose that they will offer into evidence the expert report of Dr. Kittendorf in lieu of live testimony. In addition, Plaintiffs will designate sections of the deposition of Dr. Kittendorf to be read into evidence, and Defendants will do the same, subject to the ordinary rules governing deposition designation and counter-designation. In the event that Plaintiffs object to Sandoz introducing deposition testimony from Dr. Kittendorf, Sandoz reserves the right to call Dr. Kittendorf live.

50. **Johann Gudjonsson, M.D., Ph.D. (by deposition)[38]:** Dr. Gudjonsson is a dermatologist employed at the University of Michigan and was retained as an expert for Plaintiffs in this litigation. Gudjonsson submitted a claim construction declaration and an opening infringement report and was deposed during claim construction expert discovery. Dr. Gudjonsson's testimony concerns issues relating to binding of TNF by etanercept, particularly as claimed by the Finck patents. His testimony is relevant to elements of double patenting of the patents-in-suit over the Finck patents. Despite having the opportunity to counter-designate testimony, Plaintiffs have refused to do so.

Fact Witnesses

51. **Taruna Arora, Ph.D. (by deposition):** Dr. Arora is a former Principal Scientist at Amgen, who was involved in research relating to etanercept. Dr. Arora also submitted a declaration to the U.S. Patent and Trademark Office in support of the prosecution of the '182 and '522 patents. Dr. Arora is expected to testify regarding Amgen's research relating to etanercept and the subject matter of her declaration.

52. **Patricia Beckmann, Ph.D. (by deposition):** Dr. Beckmann is a former Staff Scientist and Scientific Liaison at Immunex, who was involved in research relating to TNF receptors and etanercept. Dr. Beckmann is expected to testify regarding Immunex's research relating to TNF receptors and etanercept.

[38] Plaintiffs have chosen not to call Dr. Gudjonsson live or by deposition. Defendants intend to introduce his deposition testimony. *Vandenbraak v. Alfieri*, 2005 WL 1242158, at *1 (D. Del. May 25, 2005) ("It is proper to admit by designation "an opinion propounded by the sponsoring party's expert, whether or not the latter has come to rue it."). The introduction of Dr. Gudjonsson's testimony at trial is necessitated by Plaintiffs' position on the contested issues on double patenting. Although Plaintiffs have not offered any expert opinion disputing that, if the Finck patents were available as reference patents for double patenting, Sandoz will present unrebutted expert testimony that each of the elements of the Patents-in-Suit are met by the Finck patents' claims. Dr. Gudjonsson's testimony is relevant to elements of double patenting.

53. **Manfred Brockhaus, Ph.D. (by deposition):** Dr. Brockhaus is a former Scientific Expert at Hoffmann-La Roche, who was involved in research relating to TNF receptors. Dr. Brockhaus is a named inventor of the '182 and '522 patents. Dr. Brockhaus is expected to testify regarding the research and development of the claimed subject matter of the '182 and '522 patents.

54. **Cindy Cao, Ph.D. (by deposition):** Dr. Cao is a former Executive Director for Regulatory Affairs Biopharmaceuticals at Sandoz. Dr. Cao is expected to testify regarding regulatory issues relating to Sandoz's aBLA No. 761042.

55. **Terri Davis-Smith (by deposition):** Ms. Davis-Smith is a former Senior Research Associate at Immunex and Associate Scientist I at Amgen, who was involved in research relating to etanercept and other TNF receptor fusion proteins. Ms. Davis-Smith also submitted a declaration to the U.S. Patent and Trademark Office in support of the prosecution of the '182 and '522 patents. Ms. Davis-Smith is expected to testify regarding Immunex and Amgen's research relating to TNF receptor fusion proteins, including etanercept, and the subject matter of her declaration.

56. **Zlatko Dembic, Ph.D. (by deposition):** Dr. Dembic is a former Senior Scientist at Hoffmann-La Roche, who was involved in research relating to TNF receptors. Dr. Dembic is a named inventor of the '182 and '522 patents. Dr. Dembic is expected to testify regarding the research and development of the claimed subject matter of the '182 and '522 patents.

57. **Kathleen Fowler, Ph.D. (by deposition):** Dr. Fowler is a former Associate General Counsel at Amgen, who was involved in the prosecution of the '182 and '522 patents. Dr. Fowler is expected to testify regarding prosecution of the '182 and '522 patents before the U.S. Patent and Trademark Office.

58. **Steven Gillis, Ph.D. (by deposition)**: Dr. Gillis is a founder and former Vice President and Director of Research and Development at Immunex, who was involved in managing the drug discovery and development operations of the company. Dr. Gillis is expected to testify regarding Immunex's research relating to TNF receptor fusion proteins, including etanercept.

59. **Raymond Goodwin, Ph.D. (by deposition)**: Dr. Goodwin is a former Principal Scientist at Immunex, who was involved in research relating to TNF receptors and TNF receptor fusion proteins. Dr. Goodwin is expected to testify regarding Immunex's research relating to TNF receptors and TNF receptor fusion proteins, including etanercept.

60. **Ueli Gubler, Ph.D. (by deposition)**: Dr. Gubler is a former Senior Research Leader at Hoffmann-La Roche, who was involved in research relating to TNF receptors. Dr. Gubler is expected to testify regarding Roche's research relating to TNF receptors.

61. **Laura Hamill (live)**: Ms. Hamill is the Senior Vice President of U.S. Business Operations at Amgen, who is responsible for the commercial and business organization for all of Amgen's products in the U.S. Ms. Hamill is expected to testify regarding the commercial sale and promotion of Enbrel®.

62. **George Johnston, Jr. (by deposition)**: Mr. Johnston is the former Chief Patent Counsel at Hoffmann-La Roche, who was involved in the preparation, negotiation, and drafting of license agreements. Mr. Johnston is expected to testify regarding ownership and licensing of the '182 and '522 patents.

63. **Michael Kirschner (by deposition)**: Mr. Kirschner is a former Vice President of Intellectual Property at Immunex and Senior Associate General Counsel at Amgen, who was

involved in third-party intellectual property issues relating to Enbrel®, including patent licensing. Mr. Kirschner is expected to testify regarding patent licensing relating to Enbrel®.

64. **Tadahiko Kohno, Ph.D. (by deposition):** Dr. Kohno is a former Scientific Director at Amgen, who was involved in research relating to etanercept. Dr. Kohno is expected to testify regarding Amgen's research relating to etanercept.

65. **Leander Lauffer, Ph.D. (by deposition):** Dr. Lauffer is a former Vice President of Business Development at Behringwerke, who was involved in a collaboration with Immunex to develop TNF receptor fusion proteins. Dr. Lauffer is expected to testify regarding Behringwerke's research regarding fusion proteins, including its collaboration with Immunex to develop TNF receptor fusion proteins and etanercept.

66. **Werner Lesslauer, Ph.D. (by deposition):** Dr. Lesslauer is a former Vice Director of Research at Hoffmann-La Roche, who was involved in research relating to TNF receptors and TNF receptor fusion proteins. Dr. Lesslauer is a named inventor of the '182 and '522 patents and submitted declarations to the U.S. Patent and Trademark Office in support of the prosecution of these patents. Dr. Lesslauer is expected to testify regarding the research and development of the claimed subject matter of the '182 and '522 patents and the subject matter of his declarations.

67. **Zhengyu Liu, Ph.D. (by deposition):** Dr. Liu is a former U.S. Regulatory Lead, U.S. Biopharmaceutical Regulatory Affairs Group at Sandoz. Dr. Liu is expected to testify regarding regulatory issues relating to Sandoz's aBLA No. 761042.

68. **Hansruedi Loetscher, Ph.D. (live):** Dr. Loetscher is a former Global Head of Neuroscience Discovery at Hoffmann-La Roche, who was involved in research relating to TNF receptors and TNF receptor fusion proteins. Dr. Loetscher is a named inventor of the '182 and

'522 patents. Dr. Loetscher is expected to testify regarding the research and development of the claimed subject matter of the '182 and '522 patents.

69. **Stewart Lyman, Ph.D. (by deposition):** Dr. Lyman is a former Director of Extramural Research at Immunex. Dr. Lyman submitted declarations to the U.S. Patent and Trademark Office in support of the prosecution of the '182 and '522 patents. Dr. Lyman is expected to testify regarding the subject matter of his declarations.

70. **Mark McCamish, M.D., Ph.D. (live or by deposition):** Mr. McCamish is the former Global Head of Biopharmaceutical Development at Sandoz. Mr. McCamish is expected to testify regarding the product that is the subject of Sandoz's aBLA No. 761042.

71. **John Parise (by deposition):** Mr. Parise is the former Senior Counsel and Managing Attorney at Hoffmann-La Roche, who was involved in the negotiation and drafting of license agreements. Mr. Parise is expected to testify regarding ownership and licensing of the '182 and '522 patents.

72.

73. **Stuart Watt (live):** Mr. Watt is the former Vice President and Law and Intellectual Property Officer at Amgen, who was involved in the prosecution of the '182 and '522 patents and in the negotiation and drafting of licensing agreements. Mr. Watt is expected to testify regarding ownership and licensing of the '182 and '522 patents.

****

The above list is not a commitment that Defendants will call any particular witness at trial, or a representation that any of the witnesses listed are available, may be subject to subpoena, or will appear at trial. Defendants may offer testimony live or by deposition from the above-listed witnesses. For witnesses that will be testifying by expert report, the report will be

admitted into evidence. Defendants reserve the right to call additional witnesses (who are not presently identifiable) as may be necessary, on reasonable notice to the opposing party. In the event Defendants seek to call a substitute witness, Defendants agree to make an application to the Court to amend the Joint Final Pretrial Order.

Defendants reserve the right to call and/or cross examine any of Plaintiffs' witnesses, including by counter-designation of deposition testimony. To the extent that Plaintiffs call as a live witness any witness listed to be called by Sandoz by deposition, Sandoz reserves the right to present live testimony from that witness.

Defendants also reserve the right to call, either live or by deposition: (a) additional witnesses to provide foundational testimony should any party contest the authenticity or admissibility of any material proffered at trial; (b) substitute witnesses for any identified witnesses whose employment or other relationship with Defendants changes such that he or she is no longer able, available or willing to testify on Defendants' behalf at trial; and/or (c) additional witnesses to respond to issues raised after the submission of this list; and/or additional witnesses for rebuttal or impeachment purposes to issues raised by Plaintiffs.

For those depositions that have been videotaped, Defendants may present deposition excerpts by videotape, transcript, or both (as part of the same presentation). If any witness listed as a person who Defendants intend to call to testify in person is unavailable, Defendants reserve the right to offer deposition testimony from such witness in lieu of live testimony.

Defendants further reserve the right to introduce testimony through deposition or live examination for any witness that Plaintiffs identify on their list, for any expert witness that submitted an expert report on behalf of Plaintiffs in this action, or as necessary to establish authenticity or admissibility of any trial exhibit if the authenticity or admissibility of the exhibit

is challenged by Plaintiffs. Defendants reserve the right to offer counter-designations to any deposition designations offered by Plaintiffs. Defendants reserve the right to present testimony from any witness has been deposed in this matter.

Defendants expressly reserve the right to further modify, supplement and/or amend this Final Pretrial Order and attachments in light of issues that remain open and until entry of the Final Pretrial Order, or as otherwise permitted by the Court.

D. Plaintiffs' Objections to Defendants' Witnesses

Plaintiffs object to the presentation of deposition testimony for any witness that is within Defendants' control (as except as agreed to by the parties below) and current employees. Plaintiffs further object to Defendants assertions that Dr. McCamish may attend "live or by deposition." Plaintiffs also object to Defendants assertion that Dr. Sala may "testify regarding the research and development of the product that is the subject of Sandoz's aBLA No. 761042." Dr. Sala was designated as a Rule 30(b)(6) witness by Sandoz solely on topics related to the design-around efforts during discovery; he was not subject to a Rule 30(b)(1) deposition.

Plaintiffs also object to the admission of deposition testimony from Dr. Gudjonsson as irrelevant and misleading given the issues for which he was deposed (claim construction of the Finck Patents) is no longer at issue in this case. Defendants' designation of Dr. Gudjonsson's deposition testimony on August 17, 2018 was also untimely, as the date for exchanging deposition designations was June 26, 2018, based on the agreed schedule that the parties submitted to the Court. D.I. 499, Exhibit B.

X. DEPOSITIONS

The parties have exchanged deposition designations, counter-designations and related objections. Deposition designations, with associated objections and counter-designations are attached hereto as Appendix A (Plaintiffs' Deposition Designations) and Appendix B

(Defendants' Deposition Designations). It is expected and agreed that whichever party calls a witness by deposition will present the designated testimony as well as any counter-designated testimony.

The parties reserve their rights to supplement and amend their respective designations and counter-designations in light of any orders regarding the scope of the trial or in light of any new information submitted by the other party.

The parties further reserve their rights to present deposition testimony by any fact witness identified by the parties not excluded pursuant to any objections; supplement their designations for fact witnesses who are not available to testify at trial; and designate additional deposition testimony from fact witnesses to authenticate evidence if required. The parties may also use any and all deposition testimony, whether or not designated, for cross-examination, impeachment, or rebuttal.

The parties have agreed not to designate deposition testimony of their own expert witnesses, with the exceptions of Dr. Jones and Dr. Kittendorf. Plaintiffs will offer into evidence the expert report of Dr. Jones in lieu of live testimony. Defendants will designate sections of the deposition of Dr. Jones to be read into evidence, and Plaintiffs will do the same, subject to the ordinary rules governing deposition designation and counter-designation. Similarly, Defendants will offer into evidence the expert report and deposition testimony of Dr. Kittendorf in lieu of live testimony. Plaintiffs will designate sections of the deposition of Dr. Kittendorf to be read into evidence, and Defendants will do the same, subject to the ordinary rules governing deposition designation and counter-designation. In addition, if one side indicates at any time that one or more of its experts will not be testifying live at trial for any reason, the opposing side shall have the opportunity to designate the deposition testimony of such expert(s). Following such

designation by the opposing side, any counter-designation of deposition testimony by the expert's side shall be narrowly limited in scope to the specific issues that are the subject of the opposing side's designations. Such counter-designations shall not extend to subject matter for which the expert should otherwise have been brought to trial to provide live testimony.

Joint key to Plaintiffs' and Defendants' Objections:

Obj.	Description
AA	Asked and answered; Fed. R. Evid. 611(a)
BE	Best evidence; Fed. R. Evid. 1002
BTS	Beyond the scope of examination or of 30(b)(6) topic; Fed. R. Evid. 611, Fed. R. Civ. P. 30(b)(6)
CP	Compound question
F	No foundation or assumes facts not in evidence; Fed. R. Evid. 104, 602, 703, 901
H	Hearsay if offered for the truth of the matter asserted; Fed. R. Evid. 801, 802, 803, 805
I	Incomplete designation; Fed. R. Evid. 106, 403
IC	Improper counter designation
L	Leading; Fed. R. Evid. 611(c)
LAW	Lawyer argument or colloquy
LC	Legal conclusion; Fed. R. Evid. 701
MIS	Mischaracterization of testimony or evidence
O	Unqualified opinion testimony; Fed. R. Evid. 701, 703
OB	Attorney objection improperly designated
P	Privileged; Fed. R. Evid. 501, Fed. R. Civ. P. 26(b)(3), (4)
PK	Lack of personal knowledge; Fed. R. Evid. 602
R	Not relevant; Fed. R. Evid. 401, 402
SP	Speculation, Fed. R. Evid. 602, 701, 702
T	Improper use of deposition at trial; Fed. R. Civ. P. 32
U	Unfairly prejudicial, misleading, confusing, and/or cumulative/waste of time; Fed. R. Evid. 403

V	Vague or ambiguous; Fed. R. Evid. 611(a)
OV	Overbroad
DSFI	Document speaks for itself
NAR	Calls for a narrative
NR	Non-responsive answer
MS	Motion to strike
PE	Parol evidence
IE	Improper expert testimony

Additional Plaintiffs' Objections:

Obj.	**Description**
CU	Misleading, Confusing and/or Cumulative/Waste of time; Fed. R. Evid. 403[39]

A. Plaintiffs' Deposition Designations

1. Alliger, Peter (June 30, 2017) – **Tab A.**

2. Arora, Taruna (August 9, 2017) – **Tab B.**

3. Berndt, Christine (July 28, 2017) - **Tab C.**

4. Cao, Cindy (June 20, 2017) - **Tab D.**

5. Kohno, Tadahiko (June 15, 2017) - **Tab E.**

6. Lesslauer, Werner (May 23-24, 2017) - **Tab F.**

[39] Defendants have not agreed to Plaintiffs' proposal for a separate "CU" objection, which is duplicative of the agreed upon "U" objection based on the same Fed. R. Evid. 403. Defendants objections for "U" encompass all objections based on Fed. R. Evid. 403, including for "Misleading, Confusing and/or Cumulative/Waste of time" testimony. Defendants do not waive these objections.

7. Liu, Zhengyu (June 9, 2017) - **Tab G**.

8. Loetscher, Hansruedi (May 11 -12, 2017) - **Tab H**.

9. McCamish, Mark (June 8, 2017) - **Tab I**.

10. Oakes, Gregory (June 14, 2017) - **Tab J**.

11. Schiestl, Martin (June 7, 2017) - **Tab K**.

12. Sala, Gautier (March 9, 2018) - **Tab L**.

13. Jankowsky, Rudiger (September 20, 2013) - **Tab M**.

14. Jones, Graham (January 12, 2018) - **Tab O**.

15. Kittendorf, Jeffrey (January 16, 2018) - **Tab P**.

B. Defendants' Deposition Designations

Defendants designate the deposition testimony of the witnesses identified in **Tab N** for possible introduction as substantive evidence at trial.

1. Arora, Taruna (August 9, 2017)

2. Beckmann, Patricia (June 16, 2017)

3. Brockhaus, Manfred (May 25, 2017)

4. Cao, Cindy (June 20, 2017)

5. Davis-Smith, Terri (June 20, 2017)

6. Dembic, Zlatko (July 11, 2017)

7. Fowler, Kathleen (July 14, 2017)

8. Gillis, Steven (June 15, 2017)

9. Goodwin, Raymond (June 2, 2017)

10. Gubler, Ueli (July 7, 2017)

11. Gudjonsson, Johann (December 21, 2016)

12. Hamill, Laura (July 10, 2017)

13. Johnston, George (June 30, 2017)

14. Jones, Graham (January 12, 2018)

15. Kirschner, Michael (June 29, 2017)

16. Kittendorf, Jeffrey (January 16, 2018)

17. Kohno, Tadahiko (June 15, 2017)

18. Lauffer, Leander (May 19, 2017)

19. Lesslauer, Werner (May 23, 2017)

20. Lesslauer, Werner (May 24, 2017)

21. Liu, Zhengyu (June 9, 2017)

22. Loetscher, Hansruedi (May 11, 2017)

23. Loetscher, Hansruedi (May 12, 2017)

24. Lyman, Stewart (June 27, 2017)

25. McCamish, Mark (June 28, 2017)

26. Parise, John (June 28, 2017)

27. Watt, Stuart (June 21, 2017)

* * *

Defendants disclose these deposition designations without waiving any of its rights to modify, amend, or otherwise supplement its deposition designations. Defendants reserve the right to designate additional deposition testimony not included on this list to meet unanticipated evidence adduced at trial and/or to rebut any testimony offered or designated by Plaintiffs. Defendants reserve the right to designate additional deposition testimony not included on this list when used for cross-examination, impeachment, or rebuttal purposes. Defendants reserve the right to rely on any of Plaintiffs' affirmative designations as counter-designations. Defendants

reserve the right to designate additional deposition testimony not included on this list when used to authenticate evidence, if required. Defendants reserve the right to rely on testimony not included on this list based upon the Court's ruling on any motions filed by the parties or orders regarding the scope of the trial. Providing these designations is not a commitment that Defendants will introduce all of the designated testimony at trial. Defendants reserve the right to rely on less than the designated testimony for any reason.

XI. TRIAL EXHIBITS

The parties have exchanged trial exhibit lists and related objections.

The parties have created the attached joint trial exhibit list **(Tab WW)** of exhibits that will be deemed admitted by the Court subject to the confidentiality procedure set out by the Court at the conference on September 10, 2018.

Plaintiffs intend to introduce into evidence the exhibits listed in **Tab XX**. Defendants' objections to Plaintiffs' exhibits are also listed in **Tab XX**. Defendants reserve the right to object to any exhibit for the purpose for which it is used at trial.

Defendants intend to introduce into evidence the exhibits listed in **Tab YY**. Plaintiffs' objections to Defendants' exhibits are also listed in **Tab YY**. Plaintiffs reserve the right to object to any exhibit for the purpose for which it is used at trial.

The parties have endeavored to include on the lists at **Tab ZZ** all (i) laboratory notebooks produced by Plaintiffs in this action, (ii) documents from Roche's database of research reports produced by Roche in this action, and (iii) Sandoz's aBLA referencing ENBREL®, and thus believe the lists are exhaustive as to those documents. The parties have jointly agreed that documents listed in **Tab ZZ** are authentic and admissible, but reserve the right to object to their introduction on relevance grounds. To the extent that it is later determined that any trial exhibit falling into these categories was not included at **Tab ZZ**, the parties agree that the chart at **Tab**

ZZ will be supplemented to reflect the inclusion of such document, including documents subsequently produced.

The joint key to Plaintiffs' and Defendants' objections to proposed exhibits are as follows:

Obj.	Description
A	Authenticity; Fed. R. Evid. 901
BE	Best Evidence Rule; Fed. R. Evid. 1002
CU	Misleading, Confusing and/or Cumulative/Waste of time; Fed. R. Evid. 403
F	No foundation or assumes facts not in evidence; Fed. R. Evid. 104, 602, 703, 901
FL	Foreign Language
H	Hearsay if offered for the truth of the matter asserted; Fed. R. Evid. 801, 802, 803, 805
I	Incomplete Document; Fed. R. Evid. 106, 403
ID	Incorrect Description
LC	Legal conclusion; Fed. R. Evid. 701
LP	Admissible for a Limited Purpose; Fed. R. Evid. 105
MD	Multiple Documents
NL	Not Legible
R	Not relevant; Fed. R. Evid. 401, 402
SRM	Subsequent Remedial Measure; Fed. R. Evid. 407
SO	Settlement Offer; Fed. R. Evid. 408
U	Unfairly prejudicial; Fed. R. Evid. 403

Additional Plaintiffs' Objections:[40]

Obj.	Description
F.R.C.P.26	Outside the scope of the expert report
Unelected	Unelected references

The parties agree that any party may further supplement the exhibit list on the following schedule:

(a) Parties to exchange supplemental exhibit list on August 30, 2018 along with new exhibits identified in the supplemental exhibit list.

(b) Parties to exchange objections to the supplemental exhibits identified in the supplemental exhibit list on August 31, 2018.

Absent an extraordinary showing of good cause or based on stipulations addressed in this Final Pretrial Order in connection with supplementing exhibit lists, only the exhibits listed on the parties' exhibit lists shall be introduced at the time of trial in a party's case-in-chief and/or responsive case. The parties reserve the right to offer additional exhibits for cross-examination, impeachment, or rebuttal. The parties reserve the right to offer any exhibits listed by the other party, to the same effect as though it were listed on their own exhibit lists, including introducing such exhibits into evidence, that are not excluded pursuant to any objection. The parties reserve the right to add exhibits to this list to authenticate evidence, if required. The parties reserve the right to add exhibits to this list based upon the Court's ruling on any motions by the parties or orders regarding the scope of the trial. The parties further reserve the right to use any exhibit

[40] Defendants object to Plaintiffs' additional objections for "F.R.C.P. 26" and "Unelected references." These proposed objections were not presented to Defendants at the time the parties were exchanging exhibit objections. Defendants dispute that these are valid objections to trial exhibits.

admitted into evidence, subject to any limitations as to its admission. Any description of a document on a party's exhibit list is provided for ease of identification only and shall not be used as an admission or otherwise as evidence. The listing of a document on a party's exhibit list is not an admission that such document is relevant or admissible when offered by another party. The parties reserve the right to object to the admission of any exhibit on this list based on the claims actually tried and other evidence admitted in this case. Nothing herein shall be construed as a stipulation or admission that a document or designated testimony is entitled to any weight in deciding the merits of the case. The parties are not required to list exhibits that will be used, if at all, only for impeachment purposes.

XII. MISCELLANEOUS

The parties have agreed to the following trial procedures for the advanced notification of each witness to be called at trial, live or by designation, and all exhibits and demonstratives to be used with each such witness:

Agreement Regarding Experts: Absent a showing of good cause, any expert not listed in this Final Pretrial Order shall not be permitted to testify at the time of trial, unless the expert's deposition testimony has been properly designated and counter-designated as set forth above at Section VIII. Additionally, the curriculum vitae of every expert expected to testify at the time of trial is attached to this Final Pretrial Order. The curriculum vitae or summary of the expert's qualifications may be read into the record at the time the expert takes the stand. If a party seeks to have a summary of an expert's qualifications read into the record, that party shall provide a copy of the summary to the opposing party at the time the expert is identified as a witness that the party intends to call. The same dates and procedures for objections to demonstratives and exhibits, set forth below, shall be used regarding any objections to the summary.

Witnesses: The parties will identify by email to the opposing parties the witnesses they intend to call and the order in which they expect to call said witnesses by 7:00 p.m.[41] two calendar days before such witness will be called to testify. The email addresses of the recipients that should be emailed this information, as well as the information described in paragraphs below, shall be exchanged by the parties by no later than the date of the Pretrial Conference. The identification of witnesses shall include both live witnesses and witnesses whose testimony will be provided by deposition. For example, if the party expects to conduct the examination on Monday, notice should be given to the opposing party by 7:00 p.m. on Saturday. Each party shall update its list of expected witnesses for the following day by 7:00 p.m. at the end of each trial day, so long as the party has remaining witnesses that it intends to call on direct for that portion of the case. The parties will cooperate in good faith to keep the other side informed of the anticipated length of the questioning (both direct and cross) of each witness.

Deposition Designations: Unless otherwise agreed between the parties, the party offering deposition testimony (other than for the purpose of impeachment) shall identify the deposition testimony to be offered from previously-exchanged designations by 7:00 p.m. at least three calendar days prior to the testimony being offered into the record. A party may choose not to introduce deposition testimony designated in this Proposed Final Pre-trial Order, but may not designate additional deposition testimony after the filing of this Proposed Final Pre-trial Order absent a showing of good cause (for example, a fact witness previously expected to testify live becomes unavailable, or a party responds to testimony that presents unfair surprise or prejudice). The party receiving the designations shall inform the opposing party of any counter-designations and objections by 8:30 p.m. two calendar days prior to the testimony being offered into the

[41] Unless stated otherwise, all times are according to the Eastern Time Zone.

record, and the parties will meet and confer by 9:30 p.m. that same day. If good faith efforts to resolve the objections fail, the party objecting to the deposition testimony shall bring its objections to the Court's attention at the beginning of the following trial day. Audio and/or visual clips of the identified deposition testimony shall be exchanged by 7:00 p.m. the day prior to the testimony being offered into the record.

Exhibits: Each party will provide a list of trial exhibits to be used in connection with direct examination by 7:00 p.m. at least two calendar days before their intended use, and the receiving party will provide its list of objections no later than 8:30 p.m. the night before their intended use. The parties will meet and confer regarding any objections to such exhibits by 9:30 p.m. that same night. If good faith efforts to resolve the objections fail, the party objecting to the exhibits shall bring its objections to the Court's attention at the beginning of the trial day. Failure to comply with these procedures, absent an agreement by the parties, will result in waiver of the use of an exhibit or waiver of an objection to the exhibit.

Demonstratives: Demonstratives to be used in connection with direct examination will be exchanged by 7:00 p.m. the night before their intended use, with an agreement that any changes to the demonstratives made after such exchange will be only font/layout/format/to correct typographical errors and not edits of substance, unless made in response to and for the purpose of resolving an objection. The receiving party will provide its list of objections no later than 8:30 p.m. the night before their intended use. The parties will meet and confer regarding any objections to such demonstratives by 9:30 pm that same night. If good faith efforts to resolve the objections fail, the party objecting to the exhibits shall bring its objections to the Court's attention at the beginning of the trial day.

Demonstratives containing only trial exhibits, including with highlights, underlines, callouts, etc., need not be exchanged provided that the demonstrative is not argumentative. Demonstratives created during testimony or demonstratives used in connection with cross-examination need not be exchanged. The parties agree that copies of any demonstratives used during trial shall be submitted to the Court prior to the conclusion of trial.

Notice of Intention to Rest: By 7:30 p.m. the night before it intends to rest its case, the resting party shall give the other party notice of its intention to rest. This notice is intended to give the parties enough notice to allow them to comply with the other provisions of this order.

XIII. TRIAL COUNSEL

Plaintiffs Immunex and AML will be represented at trial by:

Liza M. Walsh
Marc D. Haefner
Christine I. Gannon
Eleonore Ofosu-Antwi
Colleen M. Maker
WALSH PIZZI O'REILLY FALANGA LLP
One Riverfront Plaza
1037 Raymond Boulevard, 6th Floor
Newark, New Jersey 07102
(973) 757-1100

David T. Pritikin (*admitted pro hac vice*)
Steven J. Horowitz (*admitted pro hac vice*)
Richard M. Chen (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
One South Dearborn
Chicago, Illinois 60603
(312) 853-7000

Vernon M. Winters (*admitted pro hac vice*)
James A. High Jr. (*admitted pro hac vice*)
Sue Wang (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 California Street, Suite 2000
San Francisco, California 94104
(415) 772-1200

Jeffrey P. Kushan (*admitted pro hac vice*)
Peter S. Choi (*admitted pro hac vice*)
Ryan C. Morris (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
1501 K Street N.W.
Washington, D.C. 20005
(202) 736-8700

Samuel N. Tiu (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 West Fifth Street
Los Angeles, California 90013
(213) 896-6000

Sona De (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
(212) 839-5300

Wendy Whiteford (*admitted pro hac vice*)
J. Drew Diamond (*admitted pro hac vice*)
Dennis Smith (*admitted pro hac vice*)
Joseph E. Lasher (*admitted pro hac vice*)
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1789
(805) 447-1000

Plaintiff Roche will be represented at trial by:

David E. De Lorenzi
Charles H. Chevalier
Christine A. Gaddis
GIBBONS P.C.
One Gateway Center
Newark, New Jersey 07102-5310
(973) 596-4500

David I. Berl (*admitted pro hac vice*)
Aaron Maurer (*admitted pro hac vice*)
Thomas S. Fletcher (*admitted pro hac vice*)
Seth R. Bowers (*admitted pro hac vice*)
WILLIAM & CONNOLLY LLP
725 Twelfth St. NW
Washington, D.C. 20005

(202) 434-5000

Defendants will be represented at trial by:

Eric I. Abraham
Christy L. Saveriano
HILL WALLACK LLP
21 Roszel Road
Princeton, NJ 08543-5226
(609) 924-0808

George C. Lombardi (*admitted pro hac vice*)
Maureen L. Rurka (*admitted pro hac vice*)
Julia Mano Johnson (*admitted pro hac vice*)
James M. Hilmert (*admitted pro hac vice*)
Dan H. Hoang (*admitted pro hac vice*)
Loren G. Rene (*admitted pro hac vice*)
Karalena M. Guerrieri (*admitted pro hac vice*)
Michael A. Meneghini (*admitted pro hac vice*)
WINSTON & STRAWN LLP
35 West Wacker Drive
Chicago, Illinois 60601-9703
(312) 558-5600

Merritt D. Westcott (*admitted pro hac vice*)
WINSTON & STRAWN LLP
1111 Louisiana Street, 25th Floor
Houston, Texas 77002-5242
(713) 651-2600

Noorossadat Torabi (*admitted pro hac vice*)
WINSTON & STRAWN LLP
275 Middlefield Road, Suite 205
Menlo Park, California 94025
(650) 858-6500

[redacted]

XV. ESTIMATED LENGTH OF TRIAL AND ORDER OF PRESENTATION

The parties estimate that trial will require approximately 35 hours for each side before the Court.[42]

The parties will provide opening statements of no more than 90 minutes per side, with Defendants presenting first and Plaintiffs presenting second. The parties will present closing statements at a time convenient to the Court. Trial shall proceed with the following order of presentation:

- Defendants will present their invalidity case;
- Plaintiffs will present their response to Defendants' invalidity case and introduce objective indicia of nonobviousness;
- Defendants will present their rebuttal on invalidity and response to Plaintiffs' presentation of objective indicia of nonobviousness; and
- Plaintiffs will present their rebuttal regarding objective indicia of nonobviousness.

* * *

The Court may amend this Order as it deems appropriate and rule on any issues as they may arise during trial.

Respectfully submitted,

Date: September 10, 2018

/s/ Liza M. Walsh
Liza M. Walsh
Marc D. Haefner
Christine I. Gannon
Eleonore Ofosu-Antwi
Colleen M. Maker
WALSH PIZZI O'REILLY FALANGA LLP
One Riverfront Plaza
1037 Raymond Boulevard, 6th Floor

[42] *See* Joint Pretrial Report. D.I. 486.

Newark, New Jersey 07102
(973) 757-1100

OF COUNSEL:

David T. Pritikin (*admitted pro hac vice*)
Steven J. Horowitz (*admitted pro hac vice*)
Richard M. Chen (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
One South Dearborn
Chicago, Illinois 60603
(312) 853-7000

Vernon M. Winters (*admitted pro hac vice*)
James A. High Jr. (*admitted pro hac vice*)
Sue Wang (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 California Street, Suite 2000
San Francisco, California 94104
(415) 772-1200

Jeffrey P. Kushan (*admitted pro hac vice*)
Peter S. Choi (*admitted pro hac vice*)
Ryan C. Morris (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
1501 K Street N.W.
Washington, D.C. 20005
(202) 736-8700

Samuel N. Tiu (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 West Fifth Street
Los Angeles, California 90013
(213) 896-6000

Sona De (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
(212) 839-5300

Wendy Whiteford (*admitted pro hac vice*)
J. Drew Diamond (*admitted pro hac vice*)
Dennis Smith (*admitted pro hac vice*)
Joseph E. Lasher (*admitted pro hac vice*)
AMGEN INC.

One Amgen Center Drive
Thousand Oaks, CA 91320-1789
(805) 447-1000

Attorneys for Immunex Corporation and Amgen Manufacturing, Limited

Date: September 10, 2018

/s/ Charles H. Chevalier

David E. De Lorenzi
Charles H. Chevalier
Christine A. Gaddis
GIBBONS P.C.
One Gateway Center
Newark, New Jersey 07102-5310
(973) 596-4500

OF COUNSEL:

David I. Berl (*admitted pro hac vice*)
Aaron Maurer (*admitted pro hac vice*)
Thomas S. Fletcher (*admitted pro hac vice*)
Seth R. Bowers (*admitted pro hac vice*)
WILLIAM & CONNOLLY LLP
725 Twelfth St. NW
Washington, D.C. 20005
(202) 434-5000

Attorneys for Hoffmann-La Roche Inc.

Date: September 10, 2018

/s/ Eric I. Abraham

Eric I. Abraham
Christy L. Saveriano
HILL WALLACK LLP
21 Roszel Road
Princeton, NJ 08543-5226
(609) 924-0808

OF COUNSEL:

George C. Lombardi (*admitted pro hac vice*)
Maureen L. Rurka (*admitted pro hac vice*)
Julia Mano Johnson (*admitted pro hac vice*)
James M. Hilmert (*admitted pro hac vice*)

Dan H. Hoang (*admitted pro hac vice*)
Loren G. Rene (*admitted pro hac vice*)
Karalena M. Guerrieri (*admitted pro hac vice*)
Michael A. Meneghini (*admitted pro hac vice*)
WINSTON & STRAWN LLP
35 West Wacker Drive
Chicago, Illinois 60601-9703
(312) 558-5600

Thomas M. Melsheimer (*admitted pro hac vice*)
WINSTON & STRAWN LLP
2121 N. Pearl Street, Suite 900
Dallas, Texas 75201
(214) 453-6500

Merritt D. Westcott (*admitted pro hac vice*)
WINSTON & STRAWN LLP
1111 Louisiana Street, 25th Floor
Houston, Texas 77002-5242
(713) 651-2600

James S. Richter
WINSTON & STRAWN LLP
200 Park Avenue
New York, New York 10166
(212) 294-6700

Noorossadat Torabi (*admitted pro hac vice*)
WINSTON & STRAWN LLP
275 Middlefield Road, Suite 205
Menlo Park, California 94025
(650) 858-6500

Attorneys for Defendants Sandoz Inc., Sandoz International GMBH, and Sandoz GMBH

IT IS SO ORDERED this 11 day of September, 2018.

Hon. Claire C. Cecchi, U.S.D.J.

CERTIFICATE OF SERVICE

The undersigned attorney certifies that a copy of the foregoing FINAL PRE-TRIAL ORDER was served by electronic mail on all counsel of record.

Dated: September 10, 2018

/s/ Liza M. Walsh

Liza M. Walsh
Marc D. Haefner
Christine I. Gannon
Eleonore Ofosu-Antwi
Colleen M. Maker
WALSH PIZZI O'REILLY FALANGA LLP
One Riverfront Plaza
1037 Raymond Boulevard, 6th Floor
Newark, New Jersey 07102
(973) 757-1100

Attorneys for Immunex Corporation and Amgen Manufacturing, Limited

OF COUNSEL:

David T. Pritikin (*admitted pro hac vice*)
Steven J. Horowitz (*admitted pro hac vice*)
Richard M. Chen (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
One South Dearborn
Chicago, Illinois 60603
(312) 853-7000

Vernon M. Winters (*admitted pro hac vice*)
James A. High Jr. (*admitted pro hac vice*)
Sue Wang (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 California Street, Suite 2000
San Francisco, California 94104
(415) 772-1200

Jeffrey P. Kushan (*admitted pro hac vice*)
Peter S. Choi (*admitted pro hac vice*)
Ryan C. Morris (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
1501 K Street N.W.
Washington, D.C. 20005
(202) 736-8700

Samuel N. Tiu (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
555 West Fifth Street
Los Angeles, California 90013
(213) 896-6000

Sona De (*admitted pro hac vice*)
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019

(212) 839-5300

Wendy Whiteford (*admitted pro hac vice*)
J. Drew Diamond (*admitted pro hac vice*)
Dennis Smith (*admitted pro hac vice*)
Joseph E. Lasher (*admitted pro hac vice*)
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1789
(805) 447-1000

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IMMUNEX CORPORATION; AMGEN MANUFACTURING, LIMITED; and HOFFMANN-LA ROCHE INC.;	)	Hon. Claire C. Cecchi
Plaintiffs,	)	Civil Action No.: 2:16-cv-01118-CCC-MF
v.	)	
SANDOZ INC.; SANDOZ INTERNATIONAL GMBH; and SANDOZ GMBH;	)	**JOINT EXHIBIT LIST**
Defendants.	)	**PRETRIAL ORDER TAB WW**

Exhibit Number	Title
JTX-1	U.S. Patent No. 8,063,182 B1 Brockhaus et al.
JTX-2	U.S. Patent No. 8,163,522 B1 Brockhaus et al.
JTX-3	File History for U.S. Patent Application No. 08/444,790 (U.S. Patent No. 8,063,182)
JTX-4	File History for U.S. Patent Application No. 08/444,791 (U.S. Patent No. 8,163,522)
JTX-5	U.S. Patent 5,610,279 to Brockhaus et al.
JTX-6	European Patent Application 90116707.2 (Manfred)
JTX-7	English Translation of European Patent Application No. 90116707.2, Publication No. 0417563A2
JTX-8	European Patent Publication No. 0417563A2
JTX-9	File History of U.S. Patent Application No. 08/095,640 (U.S. Patent No. 5,610,279)
JTX-10	File History of U.S. Patent Application No. 07/580,013
JTX-11	European Patent Application No. EP 90116707
JTX-12	Accord and Satisfaction, dated 6/7/2004
JTX-13	License Agreement for Etanercept Among Immunex Corporation, Hofmann-La Roche Inc., and F. Hoffmann-La Roche Ltd., dated 11/6/1998

Exhibit Number	Title
JTX-14	Brockhaus Clarification and Consolidation Agreement, dated 6/7/2004
JTX-15	Commercial Exploitation Agreement, dated 1/1/2015
JTX-16	Corrected Declaration of Jeffrey D. Kittendorf, Ph.D., with Exhibits A-E
JTX-17	Rebuttal Expert Report Of Graham B. Jones, Ph.D., with Exhibits 1-4
JTX-18	Kabat et al., Sequences of Proteins of Immunological Interest, U.S. Dept. of Health Services (4th Ed.) (1987)
JTX-19	Ellison et al., The nucleotide sequence of a human immunoglobulin Cγ1 gene, Nucleic Acids Research, 10(13):4071-4079 (1982)
JTX-20	Sakano et al., Domains and the hinge region of an immunoglobulin heavy chain are encoded in separate DNA segments, Nature 277:627–633 (1979)
JTX-21	Loetscher et al., Molecular Cloning and Expression of the Human 55 kd Tumor Necrosis Factor Receptor, Cell 61:351-359 (April 1990)
JTX-22	Brockhaus et al., Identification of two Types of tumor necrosis factor receptors on human cell lines by monoclonal antibodies, Proc. Natl. Acad. Sci. USA, 87:3127-31 (April 1990)
JTX-23	Dembic et al., Two Human TNF Receptors Have Similar Extracellular, But Distinct Intracellular, Domain Sequences, Cytokine, 2(4): 231-237 (July 1990)
JTX-24	Smith et al., A Receptor for Tumor Necrosis Factor Defines an Unusual Family Of Cellular and Viral Proteins, Science 248:1019-1023 (May 1990)
JTX-25	Traunecker et al., Highly efficient neutralization of HIV with recombinant CD4-immunoglobulin molecules, Nature 339:68-70 (1989)
JTX-26	Eck et al., The structure of tumor necrosis factor-α at 2.6 A resolution, implications for receptor binding, J. Biol. Chem. 264(29):17595-17605 (1989)
JTX-27	Moreland et al., Recombinant soluble tumor necrosis factor receptor (p80) fusion protein: toxicity and dose finding trial in refractory rheumatoid arthritis, J. Rheumatol. 23:1849-55 (1996)
JTX-28	Moreland et al., Treatment of rheumatoid arthritis with a recombinant human tumor necrosis factor receptor (p75)-Fc fusion protein, N. Engl J. Med. 337:141-47 (1997)
JTX-29	Moreland et al., Etanercept Therapy In Rheumatoid Arthritis: A randomized, Controlled Trial, Ann. Intern. Med. 130:478-486 (1999)

Exhibit Number	Title
JTX-30	Weinblatt et al., A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate, N. Engl. J. Med. 340:253-9 (1999)
JTX-31	Bathon et al., A Comparison of Etanercept and Methotrexate in Patients with Early Rheumatoid Arthritis, N. Engl. J. Med. 343:1586-93 (2000)
JTX-32	U.S. Patent No. 6,143,866 Brewer et al.
JTX-33	U.S. Patent No. 5,639,597 Lauffer et al.
JTX-34	Enbrel - Highlights of Prescribing Information (10/2017)
JTX-35	Slud, Patients press for Enbrel, CNN Money (2001)
JTX-36	Table 1 from Lawrence, S., Billion Dollar Babies - Biotech Drugs as Blockbusters, Nature Biotechnology 25:380-382 (2007)
JTX-37	Top 50 pharmaceutical products by global sales, for 2011-2014 PMLive
JTX-38	Top 50 pharmaceutical products by global sales, GlobalData
JTX-39	U.S. Patent No. 7,915,225
JTX-40	U.S. Patent No. 8,119,605
JTX-41	U.S. Patent No. 8,722,631
JTX-42	U.S. Patent No. 5,605,690
JTX-43	Swiss Patent Application No. CH 3319/89
JTX-44	Swiss Patent Application No. CH 746/90
JTX-45	Swiss Patent Application No. CH 1347/90
JTX-46	Engelmann, H., et al., A Tumor Necrosis Factor-binding Protein Purified to Homogeneity from Human Urine Protects Cells from Tumor Necrosis Factor Toxicity, J. Biol. Chem. 264(20):11974-80 (1989
JTX-47	Engelmann, et al., Two Tumor Necrosis Factor-binding Proteins Purified from Human Urine, The Journal of Biological Chemistry, Vol. 265, No. 3 (1990)
JTX-48	Seckinger, P., et al., Characterization of a tumor necrosis factor a (TNF-a) inhibitor: Evidence of immunological cross-reactivity with the TNF receptor, Proc. Natl. Acad. Sci. USA 87:5188-5192 (1990)
JTX-49	Stites, D., et al., Immunoglobulins I: Structure & Function, in Basic & Clinical Immunology, Ch. 4 (6th ed.1987)

Exhibit Number	Title
JTX-50	Segal, D.M., et al., The Role of Non-Immune IgG in Controlling IgG-Mediated Effector Functions, Molecular Immunol. 20:1177-89 (1983)
JTX-51	Duncan, A.R. and Winter G., The Binding Site For Clq on IgG, Nature 332:738-740 (1988)
JTX-52	Pennica, D., et al., Human tumor necrosis factor: precursor structure, expression and homology to lymphotoxin, Nature 312:724-29 (1984)
JTX-53	Shin, S., et al., Production and Properties of Chimeric Antibody Molecules, Methods in Enzymol. 178:459-476 (1989)
JTX-54	Oi, V., et al, Immunoglobulin Gene expression in transformed lymphoid cells, Proc. Natl. Acad. Sci. USA, Immunol. 80:825-829 (1983)
JTX-55	U.S. Patent 5,336,603 Capon et al.
JTX-56	Byrn, R.A., et al., Biological properties of a CD4 immunoadhesion, Nature 344:667-670 (1990)
JTX-57	European Patent Application Publication No. 0 325 262 Seed
JTX-58	Capon, D., et al., Designing CD4 immunoadhesins for AIDS therapy, Nature 337:525-30 (1989)
JTX-59	Watson, S.R., et al., A Homing Receptor-IgG Chimera as a Probe for Adhesive Ligands of Lymph Node High Endothelial Venules, J. Cell Biol., 110:2221-29 (1990)
JTX-60	European Patent Application Publication No. 0 394 827 Karjalainen
JTX-61	U.S. Patent No. 5,116,964 Capon et al.
JTX-62	European Patent Application Publication No. 0 308 378 Wallach
JTX-63	Hohmann, HP, et al., Two different cell types have different major receptors for human tumor necrosisfactor (TNFa), J. Biol. Chem. 264(25): 14927-14934 (1989)
JTX-64	Schall, T., et al., Molecular Cloning and Expression of a Receptor for Human Tumor Necrosis Factor, Cell 61:361-370 (1990)
JTX-65	U.S. Patent No. 5,395,760 Smith et al.
JTX-66	Smith, R.A., et al., The Active Form of Tumor Necrosis Factor Is a Trimer, J. Biol. Chem. 262(15):6951-6954 (1987)
JTX-67	U.S. Patent 5,447,851 Beutler
JTX-68	Peppel, K., et al., A tumor necrosis factor (TNF) receptor-IgG heavy chain chimeric protein as a bivalent antagonist of TNF activity, J. Exp. Med. 174:1483-89 (1991)

Exhibit Number	Title
JTX-69	Ashkenazi, A., et al., Protection against endotoxic shock by a tumor necrosis factor receptor immunoadhesin, Proc. Natl. Acad. Sci. 88:10535-39 (1991)
JTX-70	Crothers, D.M. and Metzger H., The influence of polyvalency on the binding properties of antibodies, Immunochemistry 9:341-357 (1972)
JTX-71	Smith, R.A., et al., Multimeric Structure of Tumor Necrosis Factor Receptor of HeLa Cells, J. of Biological Chemistry, 264(25):14646-652 (1989)